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FIVE-YEAR FOLLOW-UP STUDY OF 100 PATIENTS COMMITTED TO THE BOSTON PSYCHOPATHIC HOSPITAL

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EDITORIAL discussion in this journal of a paper on the results of treatment in the major psychoses‡ included the suggestion that "the psychiatrist could measure the effects of therapy by means of a study of 'five-year cures' much as does the student of cancer or tuberculosis." We have sought to carry out this suggestion by charting the admissions and discharges of 100 patients, week by week, for a period of five years after each original date of admission to the hospital.

Method

The names of the first 100 patients committed to the Boston Psychopathic Hospital during the fiscal year July 1, 1946, to June 30, 1947, were traced in the card-index file of the Massachusetts Department of Mental Health. Each discharge to the community, each transfer from one mental hospital to another and each readmission to a mental hospital, public and private, in Massachusetts was recorded. Each patient's sex, diagnosis, admission status — that is, whether first or subsequent admission — and treatment were also recorded.

Results

Seventy-six of the patients were presumably in the community at the end of five years (they were not in residence at any of the mental hospitals of Massachusetts, but a few might have been in mental hospitals in other states). Twelve were in mental hospitals in Massachusetts, 8 were dead, and 4 were known to be out of the State and could not be followed. The 88 patients followed for the entire five years resided in mental hospitals for an average of forty-nine weeks, or 19 per cent of the five-year period.

The original number of patients discharged to the community after treatment at the Boston Psychopathic Hospital was 70. Twenty-nine were transferred to other mental hospitals for further care, and 1 died at the Boston Psychopathic Hospital.

Table 1 shows the whereabouts, at the end of five years, of the 70 patients discharged to the community by the Boston Psychopathic Hospital, and Table 2 that of the 29 patients transferred directly to other mental hospitals.

Table 1. *Status of 70 Patients Discharged to the Community.*

Status		No. of Patients
In community		58
No readmission since discharge	38	
Intervening admission to Boston Psychopathic Hospital, with subsequent discharge	13	
Intervening admission to Boston Psychopathic Hospital, with transfer to other mental institution and subsequent discharge	7	
Unknown (patient out of State)		3
Death after readmission to Boston Psychopathic Hospital and transfer to other mental institution		3
In mental hospital		6
Boston Psychopathic Hospital	1	
Other mental institution	5	
Total		70

The whereabouts of the entire 100 patients at the end of the five-year period and the average time spent in mental hospitals during the period are presented in Table 3.

If the patients who were dead or out of the State at the end of five years are omitted from consideration the proportion of patients in the community at that point was 86 per cent (76 out of 88).

The 76 patients who were *in the community* at the end of the five years spent 10 per cent of the five years (two hundred and sixty weeks) in mental hospitals, whereas the 12 patients who were in mental

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hospitals at that point spent 76 per cent of the five-year period in mental hospitals. From this difference it appears that the fact of being in the community

TABLE 2. *Status of 29 Patients Transferred Directly to Other Mental Hospitals.*

STATUS		NO. OF PATIENTS
In community		18
No readmission since discharge from other hospital	7	
Return to other hospital after discharge, with subsequent release to community	11	
In other mental hospital		6
Intervening period in community after discharge from Boston Psychopathic Hospital	4	
No discharge from other hospital	2	
Death in other mental hospital after discharge from Boston Psychopathic Hospital		4
Unknown (patient sent out of State)		1
Total		29

five years after admission to a mental hospital is good evidence that the average patient has been able to

TABLE 3. *Status of All 100 Patients.*

STATUS	NO. OF PATIENTS	AVERAGE TIME SPENT IN MENTAL HOSPITALS wk.
In community	76	26
In mental hospitals	12	197
Dead	8	42
Unknown (patient out of State)	4	16
Total	100	
Average		47

live in the community by far the greater part of the five years.

TABLE 4. *Data in 56 Patients Hospitalized Only at the Boston Psychopathic Hospital.*

STATUS		NO. OF PATIENTS
In community*		51
No readmission†	38	
Intervening readmission to Boston Psychopathic Hospital‡	13	
Readmission, lasting till follow-up survey		1
Unknown (patient out of State)		3
Death in hospital		1
Total		56

*Average time in hospital, 14 wk.
†Average time in hospital, 10 wk.
‡Average time in hospital, 24 wk.

Fifty-six of the 100 patients had all their hospitalization at the Boston Psychopathic Hospital. Their whereabouts at the end of five years is shown in Table 4.

The most noteworthy group comprises the 38 patients who never had a readmission during the five years, for they were in hospital for an average of only ten weeks. Twenty-nine of these were women.

Forty-four patients were treated at both the Boston Psychopathic Hospital and other mental hospitals after transfer from the former. Their status at the end of five years is presented in Table 5.

TABLE 5. *Status of Patients Treated at Other Mental Hospitals after Transfer from the Boston Psychopathic Hospital.*

STATUS		NO. OF PATIENTS
In community*		25
No readmission after discharge from other mental hospital†	7	
Intervening readmission‡	18	
In other mental hospital		11
Discharge to community, with subsequent readmission	9	
No discharge to community	2	
Death in other mental hospital		7
Readmission after discharge to community	3	
No discharge to community	4	
Unknown (patient sent out of State)		1
Total		44

*Average time in hospital, 47 wk.
†Average time in hospital, 23 wk.
‡Average time in hospital, 57 wk.

Comparison of the average time of hospitalization of patients who were in the community at the end of five years who received all their care at the Boston Psychopathic Hospital with those who were treated at both the Boston Psychopathic Hospital and at other mental hospitals discloses that the former (51 patients) were under treatment for fourteen and the latter (25 patients) for forty-seven weeks (12 at the Boston Psychopathic Hospital, and 35 at other hospitals). The latter group included patients who had not improved during their Boston Psychopathic Hospital residence.

Fifty-six of the 100 patients had had no previous admission to mental hospitals. Their whereabouts at

TABLE 6. *Status of Patients Not Previously Admitted to Mental Hospitals.*

STATUS	NO. OF PATIENTS	AVERAGE TIME IN MENTAL HOSPITAL wk.
In community	40 (71%)	27
In mental hospital	9	196
Dead	5	42
Unknown (patient out of State)	2	26
Total	56	
Average		55

the end of five years and the average time in mental hospitals during the five-year period are demonstrated in Table 6.

Forty-four of the 100 patients had had one or more previous admissions to mental hospitals. Their whereabouts after five years and the average time in mental hospitals are shown in Table 7.

TABLE 7. *Status of Patients with One or More Admissions to Mental Hospitals.*

STATUS	NO. OF PATIENTS	AVERAGE TIME IN MENTAL HOSPITAL wk.
In community	36 (82%)	24
In mental hospital	3	198
Dead	3	43
Unknown (patient out of State)	2	6
Total	44	
Average		36

The number of patients who had had previous admissions was greater than that of those who had not (82 and 71 per cent, respectively). The average time of the former in mental hospitals was also considerably less than that of the latter (thirty-six as compared with fifty-five weeks).

TABLE 8. *Status of 46 Male Patients.*

STATUS	NO. OF PATIENTS	AVERAGE TIME IN MENTAL HOSPITAL wk.
In community	32 (70%)	37
In mental hospital	8	223
Dead	5	47
Unknown (patient out of State)	1	48
Total	46	
Average		70

Forty-six of the 100 patients were males. Their whereabouts at the end of five years and the average time in mental hospitals are shown in Table 8. For 54 female patients the corresponding data are presented in Table 9.

More females than males were in the community at the end of five years (81 and 70 per cent, respectively). The females, furthermore, spent less than half the average number of weeks in mental hospitals that males did.

The status of the 100 patients at the end of each year of the five-year follow-up period is demonstrated in Table 10.

TABLE 9. *Status of 54 Female Patients.*

STATUS	NO. OF PATIENTS	AVERAGE TIME IN MENTAL HOSPITAL wk.
In community	44 (81%)	17
In mental hospital	4	143
Dead	3	35
Unknown (patient out of State)	3	5
Total	54	
Average		27

A slight change occurred between the end of the first and second years, when the total number of patients in the community increased from 72 to 76. Another was observed between the end of the third and fourth years; during that interval the number of patients who had had no relapse decreased from 49 to 46. There was also an increase in the number of patients in the community who had had a relapse since the original discharge — from 27 to 31.

Patients in the last category (31 in all) had a total of 65 readmissions or an average of 2.1 readmissions apiece during the five-year period. Patients who were in the hospital but had been discharged since the original admission (10 in all) had a total of 49 readmissions; however, 1 patient had 33 readmissions. If this patient is left out patients in this group had an average of 1.7 readmissions during the five years.

The whereabouts of patients available for the entire five-year follow-up period (that is, those who had neither died nor left the State) and the proportions in each of the four groups at the end of each year are shown in Table 11.

This follow-up picture differentiates three classes of patients: those who were not discharged from mental hospital after admission; those who relapsed; and those who did not relapse. The first and third groups both decreased from the end of the first year to the end of the fifth year — 8 to 2 per cent and 59 to 51 per cent, respectively. The incidence of relapse increased from 33 to 46 per cent. It is of interest that

TABLE 10. *Status of All Patients during the Follow-up Period.*

PERIOD	PATIENTS IN HOSPITAL		DEAD PATIENTS	PATIENTS OUT OF STATE	PATIENTS IN COMMUNITY		
	NO DISCHARGE SINCE ORIGINAL ADMISSION	INTERVENING DISCHARGE & READMISSION			READMISSION AFTER ORIGINAL DISCHARGE	NO READMISSION AFTER ORIGINAL DISCHARGE	TOTALS*
End of 1st yr.	7	13	4	4	18	54	72(78%)
End of 2d yr.	5	8	7	4	25	51	76(87%)
End of 3d yr.	3	9	8	4	27	49	76(87%)
End of 4th yr.	3	8	8	4	31	46	77(88%)
End of 5th yr.	2	10	8	4	31	45	76(87%)

*Percentage of survivors followed.

although more patients relapsed in the course of the five years a smaller proportion were in mental hospitals at the end of the fifth year than at the end of the first (10 out of 41, or 24 per cent, as compared with 13 out of 31, or 42 per cent).

The proportion of patients out of hospitals was 78 per cent at the end of the first and 87 per cent at the end of the fifth year.

TABLE 11. *Status of Patients Available for Study during the Entire Follow-up Period.*

PERIOD	PATIENTS IN HOSPITAL		PATIENTS IN COMMUNITY		TOTALS
	NO DISCHARGE SINCE ORIGINAL ADMISSION	INTERVENING DISCHARGE & READMISSION	READMISSION AFTER ORIGINAL DISCHARGE	NO READMISSION AFTER ORIGINAL DISCHARGE	
End of 1st yr.	7	13	18	54	92
End of 2d yr.	5	8	25	51	89
End of 3d yr.	3	9	27	49	88
End of 4th yr.	3	8	31	46	88
End of 5th yr.	2	10	31	45	88

TABLE 12. *Status of 44 Patients with Schizophrenia.*

STATUS	NO. OF PATIENTS	PERCENTAGE OF TOTAL	AVERAGE TIME IN MENTAL HOSPITAL mo.
In community	34	77	31
In mental hospital	6	14	209
Dead	1	2	50
Unknown (patient out of State)	3	7	5
Total	44		
Average			54

OUTCOME IN RELATION TO DIAGNOSIS

Schizophrenia

Forty-four patients had schizophrenic psychosis, including 3 with paranoia and paranoid condition. Their whereabouts at time of follow-up study and the average time in mental hospitals are shown in Table 12.

TABLE 13. *Status of 30 Patients with Affective Psychosis.*

STATUS	NO. OF PATIENTS	PERCENTAGE OF TOTAL	AVERAGE TIME IN MENTAL HOSPITAL mo.
In community	25	83	15
In mental hospital	2	7	168
Dead	2	7	27
Unknown (patient out of State)	1	3	48
Total	30		
Average			27

Affective Psychosis

Thirty patients had affective psychosis, including 11 with involutional, 10 with manic-depressive and 9 with undiagnosed psychosis. Their whereabouts at the end of five years and the average time spent in mental hospitals are demonstrated in Table 13.

Toxic and Organic Psychosis

There were 20 patients who had psychosis with demonstrable toxicity or brain damage. This group comprised 12 with general paresis, 4 with alcoholic psychosis, 1 with psychosis with epilepsy, 1 with psychosis with organic changes of the central nervous system and 2 with psychosis due to drugs. Table 14 shows the whereabouts and the average time in mental hospitals.

TABLE 14. *Status of 14 Patients with Toxic and Organic Psychosis.*

STATUS	NO. OF PATIENTS	PERCENTAGE OF TOTAL	AVERAGE TIME IN MENTAL HOSPITAL mo.
In community	12	60	31
In mental hospital	3	15	214
Dead	5	25	47
Total	20		
Average			61

Miscellaneous Mental Disorders

Six patients were placed in this group; 4 had psychoneurosis, and 1 psychosis with psychopathic personality; 1 was without psychosis. The data in these cases are presented in Table 15.

DISCUSSION

Introduction of the time factor in the study of outcome of psychoses discloses information of great practical value in predicting the amount of custodial care

TABLE 15. *Status of 6 Patients with Miscellaneous Disorders.*

STATUS	NO. OF PATIENTS	PERCENTAGE OF TOTAL	AVERAGE TIME IN MENTAL HOSPITAL mo.
In community	5	83	25
In mental hospital	1	17	128
Total	6		
Average			43

that any given psychotic reaction will require. The time patients are able to remain in the community is also at least a presumptive measure of their capacity to behave in a manner tolerable to society at large. From a humanitarian point of view time spent in the community is a measure of the patient's freedom to enjoy the same privileges as other citizens. We do not yet know if there is any critical period that correlates with theoretically conceived criteria of complete recovery. We do know from other follow-up studies in preparation and from our outpatient clinic that some patients continue to improve after release from the hospital. We also know that among those who are giving good service in a variety of occupations some harbor delusions and others suffer from episodes of disturbing anxiety. Their behavior, however, is no more abnormal than that of many people whose sanity has never been questioned.

The data presented in this study indicate that 9 out of 10 psychotic patients committed to mental hospitals can be discharged to the community, and that approximately 8 out of 10 will be in the community five years after admission, having spent on the average half a year in mental hospitals. The data further disclose that there are essentially three categories of patients: those who do not respond to treatment (about 1 out of 10 patients); those who respond quickly — that is, within an average of ten weeks, and never return to a mental hospital within a five-year period (about 4 out of 10 patients); and those who respond more slowly to treatment, have on an average of two relapses in five years and spend an average of about one year out of the five in mental hospitals (about 4 out of 10 patients).

The most unexpected finding of this study is that more than three quarters of the schizophrenic patients were in the community five years after admission, having spent less than an average of eight months in mental hospitals. Whether this result can be ascribed to the accuracy of the frequently voiced opinion that the Boston Psychopathic Hospital receives patients sooner after the inception of their psychosis than other hospitals is an open question. If so, these results indicate that there are many patients with schizophrenia (as we conceive the diagnosis) who have the capacity to return to live in the community for relatively long periods. In the past, undervaluation of recovery potential and absence of treatment combined to induce psychiatrists to hold schizophrenic patients under custodial care for long periods. Detention in the closed wards of mental hospitals may well have contributed to the deterioration that was expected in schizophrenia. Modern somatic treatments and attention to emotional needs alleviate many states of fear, depression and excitement, enable patients to resume relations with other people and make possible their discharge to the community. It cannot yet be predicted accurately in individual cases how long patients will continue to get along with others. The results of this study strongly suggest that, on the whole, they can get along for longer periods than is generally recognized.

The outcome of patients with toxic and organic psychosis was also unexpected, but this sample was small. Three fifths of the patients were in the community five years after admission, having spent an average of less than eight months in mental hospitals. This result is largely a reflection of the effectiveness of fever treatment and penicillin in general paresis.

It is common knowledge that affective psychoses respond readily to electric shock. The results of this study indicate that over four fifths of patients admitted with affective psychoses were in the community five years after admission, having spent an average of only fifteen weeks in mental hospitals. Of the 25 patients in the community at the end of five years, 16 had never had a readmission, 6 had had 1 readmission, and 3 patients had had 2, 3 and 4 readmissions apiece. Owing to the relatively large number of patients who were not readmitted to a mental hospital the average number of readmissions during the five-year period was less than 1 — namely, 0.6.

SAFE CONDUCT OF THE PATIENT THROUGH CARDIAC SURGERY (Concluded)*

With Special Reference to Diseases of the Mitral and Aortic Valves

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BOSTON

IMMEDIATE POSTOPERATIVE CARE

After a cardiac operation the general measures included in the care of all patients subjected to thoracic surgery apply. The altered physiology of the open wound of the chest is corrected by an air-tight closure of the chest wall, re-expansion of the lung and continued evacuation of fluid and air through water-sealed drainage tubes. In all cases a posterolateral tube just above the diaphragm will evacuate fluid. When there is any air leak from damaged lung, a second tube may be brought out through the second

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intercostal space anteriorly. Tubes are removed when they cease to function, generally, within forty-eight hours.

Fowler's Position

At the end of the operation, as soon as the dressing is in place, the patient is turned on his back, and the head of the table elevated. He is then maintained in Fowler's position regardless of the presence or absence of detectable peripheral blood pressure. There seems to be no evidence that cerebral anoxia will result if the head is elevated in shock. Furthermore, there is no question that the patient ventilates much more satisfactorily when the weight of the viscera is removed from the diaphragm and gravity does not contribute to pulmonary congestion. An important exception to this rule, however, has been pointed out by Hufnagel.[16] He has noted that after his plastic valve has been placed for the correction of aortic insufficiency the patient does much better flat or in the Trendelenburg position.

Oxygen Administration

As in all intrathoracic procedures oxygen should be administered by nasal catheter for the first twenty-four hours. It may then be discontinued if its omission does not result in an elevated pulse or respiratory rate, or both. The special undesirability of anoxia in the cardiac patient dictates longer oxygen administration if there is hypotension, cyanosis or any other evidence of impaired circulation. In many of the poor-risk patients it is best to continue oxygen for four or five days. Oxygen masks are not used because of the discomfort to the patient and the impracticability of keeping them in proper functioning position. Oxygen tents have also been abandoned owing to the notorious difficulty of maintaining a satisfactory concentration of oxygen.

Antibiotics

At the end of the operation 1,000,000 units of penicillin and 1 gm. of streptomycin are placed in the pleural space. Procaine penicillin G is continued by the intramuscular route for seven to ten days. The continuation of streptomycin does not appear necessary, and the occasional case of vestibular damage will be avoided by its omission.

Elastic stockings are applied postoperatively on all patients to reduce venous stasis and thus the danger of pulmonary emboli.

Sedation

In the immediate postoperative period these patients often have considerable pain from pressure on or trauma to the intercostal nerves. The surgeon can reduce this by crushing two nerves above and two below the incision at the time of operation. Morphine should be administered in sufficient dosage to allow the patient to cough comfortably, but depressive amounts must obviously be avoided. If this is not done the patient will not cough effectively and clear his increased tracheobronchial secretions.

Retained Secretions

The patient with pulmonary vascular congestion secondary to heart disease has an even greater tendency to atelectasis than the average patient after a thoracic operation and demands particular attention to these details. He should frequently be put in the sitting position to cough, with someone supporting the operated hemithorax with the flat of the hands. If this does not result in clearing of rales and rhonchi, if the cough remains wet, if x-ray studies reveal atelectasis or if the temperature and pulse remain elevated, nasotracheal suction should be begun. This is frequently necessary on the day of operation and should be employed early and as often as necessary to eliminate the signs of retained tracheobronchial secretions mentioned above. If this fails bronchoscopy may be necessary. During tracheal suction frequent rest periods with oxygen administered down the catheter will avoid the serious anoxia that can be particularly hazardous to the patient with limited cardiac reserve.

Ambulation

Early ambulation favors rapid re-expansion of the lung and more effective cough. It should be practiced except when the patient's age, cardiac status or general condition is a contraindication. Ambulation is delayed in the patients with Group 4 mitral stenosis[6] and after the correction of mitral insufficiency. After a cardiotomy in the left ventricle the patient is kept at bed rest for two weeks and treated as though he had had a myocardial infarction.

Within a few days of operation the patient is instructed in breathing exercises to mobilize the operated hemithorax. Arm raising is practiced to avoid "frozen shoulder." These exercises are continued for a month.

Hypotension

In a certain number of cardiac patients hypotension may be a problem immediately after operation. This is treated with adequate blood replacement as described above. Too often drainage of blood from the chest tube is overlooked; determination of its hematocrit will serve as a guide to replacement. In addition it may be necessary to administer nor-epinephrine to maintain a blood pressure sufficient to perfuse the coronary vessels. When it is necessary to use this agent after operation it should not be injected into a limb that has had a previous arterial infusion lest skin slough from arterial spasm occur. Damaging peripheral constriction may occur, however, even in the absence of a previous arterial cutdown. If admin-

istration results in blanching and coldness of the extremity the use of another extremity or a change to Neosynephrine intramuscularly is indicated.

Hyperpyrexia

In some patients, despite the most careful tracheal suction, high fever may occur, and in such cases aspirin by mouth, rectum or vein is indicated to eliminate the tachycardia of hyperthermia, which may impose an undesired burden on the myocardium. Nicotinic acid in an infusion may help produce a cooling vasodilatation. Dehydration must also be considered as a possible cause of this condition although it seems reasonable to postulate minute emboli to the temperature-regulating centers of the brain stem in at least some of the cases. Experience with hyperpyrexia resulting from other lesions of the central nervous system suggests that the administration of Compound F or cortisone may be effective in reducing the temperature.

Digitalis

The previously determined maintenance dosage of digitalis must be given during the morning of operation and continued without interruption. For the first few postoperative days the parenteral routes of administration should be employed whenever there is any question of intestinal absorption. In a significant number of patients rapid fibrillation will develop either during operation or shortly thereafter. This will necessitate the supplementation of the maintenance dose of digitalis with short-acting preparations such as Digoxin (0.25 to 0.5 mg.) orally or intravenously or Cedilanid (0.2 to 0.4 mg.) intravenously or ouabain (0.1 to 0.2 mg.) intravenously. If the apical rate remains above 120 these agents should be administered every two or three hours until slowing occurs. Prostigmine will temporarily control the rate, but supplementary digitalis in some form will eventually have to be given.

In all cases of uncontrolled rate an electrocardiographic tracing will help rule out digitalis toxicity as the cause of the tachycardia. In actual practice the vast majority of such patients require additional digitalis, but when the situation is unclear the use of the ultrashort-acting acetyl strophanthidin[17] under careful electrocardiographic control may be helpful. From 0.2 to 0.4 mg. of this agent is given intravenously, and the electrocardiogram followed. Slowing of the cardiac rate is a clear indication for supplementation of digitalis; if evidence of myocardial toxicity is seen further digitalis should be withheld. The usefulness of this agent lies in the fact that its effect is generally dissipated within half an hour. It is a dangerous drug, however, and must be used with great caution. A similar diagnostic test can be performed with Digoxin, Cedilanid or ouabain.

Quinidine

In all patients with mitral stenosis in regular rhythm and in all who have undergone a transventricular cardiotomy quinidine (0.2 gm. every four hours) is given prophylactically after operation. Since the patient reacts promptly from his anesthetic, oral medication can be instituted immediately after the procedure. Before this policy was adopted about 75 per cent of the patients undergoing valvuloplasty who were in normal rhythm fibrillated after operation. The institution of prophylactic postoperative quinidine has reduced the incidence of this complication, which has not been eliminated entirely, however.

If the atrial fibrillation occurs in spite of prophylactic administration of quinidine this drug is discontinued. Then, after a week or ten days, the rhythm can often be restored to normal by a program of gradually increasing quinidine dosage. Various schedules of quinidine administration have been advocated for this purpose.[18] One that we have found useful begins with 0.2 gm. every two hours for 5 doses. If this does not result in conversion to normal rhythm the administration of 0.4 gm. every two hours for 5 doses is repeated on the following day. Even at this dosage repeated electrocardiographic observation for signs of toxicity is necessary; the drug is discontinued if ventricular tachycardia, ventricular slowing, ventricular extrasystoles, prolongation of the QRS complex to more than 25 per cent of the control value or a significant lengthening of the PR interval appears. It should be emphasized that the occurrence of gastrointestinal symptoms or tinnitus bears no relation to the quinidine blood level or to the toxic effect of the drug on the heart. If 5 doses of 0.4 gm. are unsuccessful and none of the signs of myocardial toxicity mentioned above are present larger doses can be given, with the realization that they carry a distinct risk.

Heparin

Heparin is generally administered, after operations for mitral stenosis, to patients with heavily calcified and clumsy leaflets to prevent the formation of fresh clot with the implied threat of late embolization. In the vast majority, in whom adequate mobilization of the valve leaflets has been obtained by satisfactory valvuloplasty, however, this is not necessary. A similar rationale indicates heparin prophylactically after the correction of aortic stenosis, for these valves are almost invariably heavily calcified. Heparin is likewise employed when pulmonary embolization occurs postoperatively, particularly in patients with long-standing congestive heart failure. The dosage varies from 40 to 75 mg. every six hours and must be regulated by frequent determinations of the clotting time.

Arterial Embolization

If a noncritical arterial embolism (other than cerebral) occurs conservative management with heparin

is generally indicated, but it is occasionally necessary to perform embolectomy for large saddle emboli of the aorta. Fortunately, if a good valvuloplasty has been performed the patient tolerates further surgery well, even on the day of the cardiac procedure.

Cerebral emboli have been reduced by obstruction of the circulation to the brain during the hazardous portions of valvuloplasty and by vigorous flushing of the atrium before the finger is inserted. The dangerous times are during the intracardiac manipulation in clotted atria or in the presence of a calcified valve. When emboli occur in spite of precautions heparin is withheld, for it may accentuate the cerebral damage by further perivascular extravasation of blood. The treatment is supportive, with emphasis on oxygen therapy and physiotherapy to any paralyzed extremities.

Water and Electrolyte Management

At present the problems of water and electrolyte imbalance are second only to cerebral embolization as sources of morbidity and mortality after operations on the mitral valve. Previous experience in cardiology and thoracic surgery, unfortunately, is not applicable to the unique problems of this group of patients. Moore and Ball[19] have ably described the normal response to trauma or surgery in the healthy adult. This consists predominantly of the early retention of sodium, lowered serum sodium levels and loss of weight during a period of negative nitrogen and potassium balance. After cardiac operations these tendencies, probably because of tissue anoxia, are greatly accentuated and require special attention. Everyone working in the field of cardiac surgery has frequently observed a marked fall in serum sodium concentration by the second postoperative day. The lowest value with survival observed in this series was 109 milliequiv. per liter, and many have been in the range of 117 to 125 milliequiv. Metabolic and isotope-dilution studies[2] have made a significant contribution to cardiac surgery in defining the nature of this derangement and placing its therapy on a rational basis. The total exchangeable sodium and potassium and total body water have been determined in patients before and after cardiac surgery. These studies have shown that a knowledge of the "total" body composition of these elements is a key to the understanding and proper management of the postoperative changes.

Three possible explanations for the low serum sodium seen after operation suggested themselves: shift from serum into cells; dilution of the serum; and depletion of the body stores of sodium.

Shift from serum into cells. The earlier work of Moore and Ball[19] indicated shift of sodium from serum into cells as a probable explanation for the moderate hyponatremia characteristically seen after trauma or operation. Since this mechanism is probably the least controllable investigation of the other two possibilities seemed indicated as well. It is quite probable, however, that "shift" plays a significant role in the cardiac patient after operation.

Dilution of serum. One of the most important observations from the balance studies is the remarkable and unique tendency of cardiac cripples to accumulate body water when fluid intake is not restricted after operation. Instead of the usual steady fall of body weight after a surgical procedure these patients show a distinctly abnormal gain in weight, even in the absence of salt intake. The resulting increase in body water may then contribute to the hyponatremia by serum dilution. Undoubtedly, the tendency to ingest excess fluid is encouraged by the surgeon who erroneously assumes that the oliguria, which is virtually universal after cardiac surgery, is due to dehydration. Comparison of the daily weight with the preoperative level, however, exposes this fallacy. Study of a large group of cardiac patients revealed that as water intake increased over 1500 cc. per twenty-four hours there was no appreciable gain in urinary output. In fact, in one characteristic patient this fluid accumulation amounted to 7 liters in three days. Antidiuretic factors are prominent after cardiac surgery; their origin remains obscure, but their clinical importance is obvious.

Since this tendency was identified all patients after cardiac surgery have been restricted to 1500 cc. of fluid (by the oral as well as the parenteral route, not including blood replacement) in the first twenty-four hours. On the first and second postoperative days the same amount is allowed, and the ration is not increased until the usual spontaneous diuresis occurs. Unusual size of the patient or inordinate loss by sweating in hot weather, of course, requires appropriate adjustment. Under this regimen the serum sodium seldom falls below 125 milliequiv. per liter, and the low-sodium syndrome has become uncommon.

Depletion. The final possible explanation for the severe hyponatremia is that the cardiac patient, after long periods of sodium restriction and diuresis, is actually depleted in sodium stores. Early in this experience, before the balance studies were available, many patients with postoperative hyponatremia and disorientation were given hypertonic saline solution in small amounts. On several occasions this therapy was coincident with correction of the clinical aberrations and a rise in the serum sodium level. However, in other cases it was apparent that the salt load aggravated existing congestive heart failure and, in 1 case at least, contributed to the fatal outcome.

An outstanding finding of the isotope-dilution studies, however, was that in the vast majority of cases the total exchangeable sodium was normal or high. Only 1 patient in a group of 30 extensively studied showed an actual depletion of sodium. Indeed, the combination of high body sodium and high total body water appears to be quite characteristic of the cardiac patient with or without edema and either before or after surgery. It is of interest that a low

total exchangeable potassium with a relatively high plasma potassium level is also a part of this picture.

On the basis of the balance studies it is now possible to provide several rules-of-thumb, which may be utilized as a guide in the clinical management of the cardiac patient after operation, even in the absence of isotope-dilution determinations of the actual body composition. They are as follows:

In the first place, when *surgery has been successful* in improving circulatory dynamics *and caloric intake can be resumed* the electrolyte pattern is gradually restored to normal if water and salt loading are avoided. The depressed serum sodium and elevated serum potassium revert to normal coincident with the usual diuresis on the third or fourth postoperative day. This restoration, which is merely a biochemical index of general convalescent rehabilitation, is the pattern in the majority of patients particularly if the degree of congestive heart failure is minimal.

Secondly, in patients with a greater degree of congestive heart failure and in the small group in which preoperative body wasting has been maximal surgical convalescence and caloric resumption are slow. In these cases water and salt restriction, daily weight measurement and caloric forcing are indeed life-saving measures. In addition to this program there are a few cases in which hypertonic saline solution may be useful.

Of the specific indications for the intravenous use of 250 cc. of 3.0 per cent sodium chloride the first is when the usual postoperative oliguria (200 to 400 cc. per twenty-four hours) is accompanied by a dangerously high serum potassium with associated serious cardiac irregularities (atrial flutter, sudden atrial fibrillation in a patient previously in normal rhythm, atrioventricular dissociation or atrial arrest). Hypertonic saline solution may be given as emergency therapy under electrocardiographic control to reduce the hyperkalemia and correct the resultant myocardial toxicity. This is followed by an infusion of 10 per cent glucose covered by insulin. If potassium intoxication remains severe extravascular dialysis with the artificial kidney may be life saving.

A further indication for hypertonic saline infusion is when the patient manifests hyponatremia beyond the fourth or fifth day in spite of a technically satisfactory corrective procedure. This pattern, coupled with failure of diuresis, has been found to be characteristic of a small group. In such cases, if fluid has been restricted, weight is constant or falling and caloric intake has begun, a small dose of hypertonic saline solution often initiates a gradual restoration of the plasma electrolyte pattern to normal over a period of several days and actually effects water diuresis. At the same time, the disorientation, weakness and apathy that are commonly associated may be relieved. As in the preoperative patient such saline therapy must be followed closely by measurements of body weight and serum sodium. The ideal is a rise in serum sodium with no weight gain; if weight increases and serum sodium fails to respond further salt must be withheld.

The third indication is when an acute depression of the plasma sodium concentration progresses to 120 milliequiv. per liter or below within forty-eight hours of operation and there are associated symptoms (disorientation, depression and hypotension). Here, again, a single dose of hypertonic saline solution given with caution may be of emergency value for acute hyponatremia even though it exaggerates the high body sodium present in the majority of patients. This situation has been rare.

Finally, in cases in which the surgery is not considered to have resulted in much improvement and the caloric intake remains limited the electrolyte pattern remains distorted. In our experience a wide variety of maneuvers aimed at "passive" restoration of water and electrolytes to normal are quite unavailing. Indeed, salt loading in these circumstances may seriously aggravate the situation, and restoration of body composition to normal is a virtual impossibility. Indeed, the ability of the body to restore its composition to normal after a cardiac operation is one of the most significant evidences of success. And, conversely, when surgery cannot be undertaken or is unsuccessful it is futile to attempt to "improve" serum composition with a failing heart.

Adrenal Failure

On a few occasions in which intractable hypotension that could not be explained on a more usual basis was encountered postoperatively adrenal failure has been suspected. The patient is alert and oriented despite the absence of detectable blood pressure. An eosinophil count reveals the lack of the anticipated postoperative fall. Compound F intravenously may prove life saving in such cases. Intramuscular injection of cortisone is not dependable because of unreliable absorption in the hypotensive state and ACTH is of no value because the defect is in adrenal response.

Management after Discharge

The Psyche

During the period immediately after operation and discharge from the hospital serious attention must be given to a reorientation of the patient's outlook. Limitation of physical activity has long been a proper cornerstone of good medical management of the cardiac patient. Even in the patient with Group 3 mitral stenosis[6] severe restriction of activity not only has been urged but also has been a practical necessity. A certain number of patients may interpret the repeated admonitions to rest as proof of permanent disability.

After a successful cardiac operation this attitude must be corrected. A patient who does not know that he is better will not enjoy the advantages of his improvement. Beginning with his ascent through the twilight zones of anesthesia, he is repeatedly reassured, but only, of course, when this is consistent with fact. In this way his outlook is reoriented from the start to a realization that he is better. When he finds that he can climb stairs with minimal effort at the end of a week after a satisfactory valvuloplasty he is further reassured that his new confidence is solidly based.

Careful attention to all these matters will bring the sick cardiac patient through a major operation and contribute to his discharge from the hospital in improved condition. The two weeks immediately after the procedure, however, are not the only important ones. The patient must be managed with great care for several months as his myocardium, lungs and liver become adjusted to the new circulatory dynamics. During this period continued salt restriction, digitalis, diuretics and rational restriction of activity are mandatory under careful supervision. Even the good-risk patient with mitral stenosis who enjoys a brilliant early result from valvuloplasty cannot be discharged to his own devices; although some need constant encouragement, others must be warned about overtaxing their convalescing myocardium. The analogy can be made to a limb that has been in a cast for several months: when it is removed, the muscles require retraining and cannot be expected to resume full activity immediately. The same precaution obviously applies to the myocardium of the left ventricle that has been splinted from activity by the stenotic dam. However, abuse of this muscle has much more serious implications.

Digitalis and Salt Restriction

In patients in atrial fibrillation in whom reversion to normal rhythm is contraindicated (patients with persisting clots in the left atrium) digitalization must be maintained indefinitely. The same statement is true of patients with multivalvular lesions and those with Group 4 disease who have had intractable congestive heart failure. In patients who maintain or are reverted to normal sinus rhythm, however, the digitalis may be omitted after several months, and salt restriction relaxed. This should be done only if the patient is tolerating a normal level of activity satisfactorily, and both should be reinstituted if any symptoms appear. It must be remembered that progressive improvement after a satisfactory valvuloplasty often continues for a year or more but that this improvement is almost invariably sustained.

Physical Activity

As a general rule the patient is advised to limit his activities when either fatigue or dyspnea appears. As time progresses his horizon gradually expands without his having overtaxed his recuperative powers.

Diuretics

A single dose of a mercurial diuretic is routinely given at the time of the first postoperative visit (usually within a month of operation). If there is liver enlargement, pleural or alveolar fluid or peripheral edema this is repeated at weekly intervals, with ammonium chloride administration when indicated, until the patient no longer responds with a significant increase in urine volume. In the majority of cases one or two doses are all that are required, but in the patient with Group 4 disease this program may continue for many months.

Quinidine and Reversion to Normal Rhythm

Quinidine prophylaxis (1.0 to 1.5 gm. a day in 4 divided doses) is maintained for six weeks to two months in all patients who were in normal rhythm before operation so that the period of atrial irritability may be safely passed. After this time the inflammatory reaction around the atrium can be assumed to have subsided. In cases with transient fibrillation after operation but with subsequent reversion to normal rhythm it is probably safer to continue this dosage for four to six months.

The question whether to attempt reversion of chronic fibrillation to normal rhythm after successful valvuloplasty is currently being examined. Enough experience has been obtained for one to conclude that many patients will gain a significant increment of exercise tolerance by this means and a good result can thus be transformed into a brilliant one. Hansen and his co-workers[20] have demonstrated by cardiac catheterization an increase in cardiac output of over 10 per cent after conversion to normal rhythm in 9 of 14 patients studied.

In a similar catheterization study Hecht et al.[21] found that, on the average, the cardiac output on exercise increased, pulmonary ventilation fell and the arteriovenous oxygen difference returned toward normal after conversion to normal sinus rhythm. They concluded that "coordinate contraction of the cardiac atria aids in cardiac filling during demand periods and that this reserve function is lost in auricular fibrillation."

Obviously, the presence of clot in the left atrium at the time of operation constitutes a contraindication to reversion. At present a past history of embolization is not considered a contraindication to reversion if no clot has been found at the time of cardiotomy. Admittedly, clots could be sequestered in unexplored portions of the left atrium, but in this experience significant intra-atrial clot has invariably been associated with a thrombus in the appendage. The concomitant use of anticoagulants for a week before and during reversion seems advisable despite the fact that in several large series of cases the rhythm has been restored to normal without their use and without significant incidence of embolization.

In general this procedure should be reserved for the patient who has had a technically satisfactory valvuloplasty and is free of other significant valvular lesions. In some patients an attempt may be made before they are discharged from the hospital; it may be better to readmit others for reversion after several months of convalescence. The dosage schedule is described above in the section on quinidine in the immediate postoperative care.

Penicillin Prophylaxis[27-35]

After the demonstration that small doses of penicillin were effective in preventing recurrences of rheumatic fever in children it became routine to place all patients with rheumatic valvular disease on oral penicillin prophylaxis after operation. The dosage employed may be varied within wide limits, but the regimen that appears most reliable in terms of patient co-operation without sacrifice of efficacy is the administration of 200,000 units of penicillin orally once a day at least an hour before or three hours after a meal. In young patients or those in whom there is suspicion or demonstration of rheumatic activity this program should extend throughout the year for a period of five years. In others protection during the months of respiratory infections appears adequate. All patients are instructed to take 800,000 units of penicillin in 4 divided doses daily on the day before, the day of and the day after any dental work or for any sore throat or pulmonary or other infections since it appears reasonable to assume that the roughened valve leaflets are still subject to subacute bacterial endocarditis in spite of the improved cardiovascular dynamics.

Summary and Conclusions

This detailed discussion has been presented not to alarm the physician who is newly faced with these problems and not to impress those already active in this field but rather to promote an understanding of the complexity of the care of a cardiac surgical patient and to present the medical aspects in proper perspective. Indeed, these surgical procedures are improperly managed if they are regarded as a "tour de force" in which the surgeon merely performs a rapid and dramatic intracardiac maneuver with no regard to detailed care before and after operation.

In short, this discussion has attempted to emphasize not only the importance of good technical surgery but also the far greater complexity of the total care of the patient in which the operation per se is only an incident. We shall have served our purpose if we have called attention to the vital importance of medical care before the procedure and for long periods, even years, afterwards.

The views expressed are the synthesis of the thoughts and contributions of many persons, noteworthy among whom are Drs. C. Sidney Burwell, William S. Derrick, Lewis Dexter, Laurence B. Ellis, Eugene C. Eppinger, Harold D. Levine, Samuel A. Levine and Francis D. Moore.

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CARCINOMA OF THE PINNA*

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CARCINOMA of the pinna as a disease of surgical importance has received little attention in the American literature. It represents about 5 per cent of all skin cancers,[1-3] 7 per cent of epitheliomas of the head and neck[3,4] and 25 to 33 per cent of epidermoid carcinomas of the head.[4,5] More than half the lesions of the pinna are epidermoid carcinomas, and of these 8 to 15 per cent metastasize to the regional lymph nodes.[1-3] Surgery,[4,8] irradiation,[1,2,6] various dermatologic technics[3] and "chemosurgery"[7] are reported to have produced three-year "cure rates" of 60.0 to 82.5 per cent, when estimated according to the method of Martin, MacComb and Blady.[9] The relatively poor results of treatment of this readily visible skin cancer in an unessential organ have led me to re-examine the problem.

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Material

From 1930 to 1948, 230 previously untreated skin cancers of the pinna were seen at the tumor clinics of the Collis P. Huntington Memorial Hospital and the Massachusetts General Hospital. All were proved pathologically, and all received definitive treatment at these institutions. One hundred and sixty-six lesions (Table 1) were classified as determinate and were available for analysis. All patients were seen before treatment by a team representing the surgical, radiologic and dermatologic services. Follow-up examinations were performed at intervals of one to three months during the first year and less often thereafter. At the end of a three-year period of observation 151, or 90.91 per cent, were considered cured. Of these, the lesions subsequently recurred in 2 cases, and at the end of five years 93, or 84.5 per cent, of the 110 cases then regarded as determinate were considered cured.

Table 1. *Analysis of 230 Primary Carcinomas of the Pinna.*

Classification	No. of Cases
Indeterminate (at 3 yr.):	
Death without disease in less than 3 yr.	27
Untraced	37 (16%)
Total	64
Determinate (at 3 yr.):	
Considered cured	151 (90.91%)
Failures	15
Total	166
Indeterminate (at 5 yr.):	
Death without disease (3-5 yr.)	27
Untraced	29
Total	56
Determinate (at 5 yr.):	
Considered cured	93 (84.5%)
Failures	17
Total	110

Race, Sex and Age

The 166 primary lesions were encountered in 154 patients, all of whom were Caucasian. There were 134 males and 20 females. The average age at onset was sixty-eight and a half years. Age seemed to bear no relation to the outcome of treatment, to the pathology of the lesion or to the rate of recurrence or metastasis.

Occupation and Possible Etiologic Factors

In 114 cases, including 8 female patients, there were other skin cancers or multiple keratoses. Eighty-seven of the males had occupations entailing considerable exposure to sun and weather. Of these, 20 gave a definite history of frostbite of the involved pinna. Seventeen gave a history of exposure to possibly carcinogenic agents. Four other patients reported exposure to arsenic compounds, in the form of sprays, but did not show arsenical dermatoses. One patient with arsenical dermatosis and cancer of the pinna had previously taken Fowler's solution. In 7 male patients cancer developed at the site of irritation from the bows of spectacles. Occupation and possible etiologic agents had no striking relation to the results of treatment.

Treatment

The initial treatment of 133 lesions was by some surgical measure, and there were 8 recurrences (Table 2). The type of surgery varied with the extent of the disease from simple skin excision in early, small lesions, to the usual V excisions in more advanced lesions and amputation of the pinna, with radical mastoidectomy and partial parotidectomy, in the extremely advanced cases.

Thirty-three patients received some type of radiation therapy as their first treatment. In 3 cases, treatment was palliative only. Of the remaining 30 there were recurrences in 18 (Table 2). Many of the earlier patients received their irradiation in the form of exposure to radium, and in these the dosage varied from 6 to 25 millicurie hours. X-ray therapy varied from 2000 to 7000 r in single or divided doses. After irradiation there were 3 cases of massive radionecrosis that required extensive plastic reconstruction. Thirty per cent of all patients treated by irradiation complained at some time of troublesome, persistent perichondritis.

Table 2. *Treatment and Results after Three Years (Recurrences Pathologically Proved).*

Type of Therapy	No. of Cases	Recurrences	
		No.	Percentage
Initial treatment:			
Surgery	133	8	6.0
Irradiation	33	21	63.6
Treatment of local recurrence:			
Surgery	30	15	92.0 50.0
Irradiation	25	23	

In all, there were 55 pathologically proved local recurrences (29 cases) after treatment one or more times by surgery or irradiation or both (Table 2). Thirty recurrences were treated surgically, and 15 of these patients were considered cured three years after their last treatment. Twenty-five received irradiation, and only 2 were ultimately considered cured.

Pathology

There were 71 basal-cell lesions, with 64 three-year cures. In 12 mixed or basosquamous lesions, there

were 11 three-year cures. Of 83 epidermoid carcinomas 76 were considered cured at the end of three years. According to Broders's[8] classification the epidermoid carcinomas were broken down as follows: Grade 1, 47 cases; Grade 2, 29 cases; Grade 3, 6 cases; and Grade 4, 1 case. The results of treatment were the same for the three main tumor types although those of higher grade had less satisfactory results (Table 3).

Four epidermoid carcinomas metastasized to the regional lymph nodes. Of these, 1 was Grade 1, 2 were Grade 2, and 1 Grade 4. Two basosquamous carcinomas metastasized to the regional lymph nodes. One cure resulted from a regional-lymph-node dissection, and 3 failures followed irradiation of metastases. In 2 other cases the metastases were not treated.

TABLE 3. *Pathology, Stage of Disease and Results after Three Years.*

TYPE OF CARCINOMA	STAGE 1 NO. OF CASES	STAGE 2 NO. OF CASES	STAGE 3 NO. OF CASES	TOTALS	CURES	METASTASES
Epidermoid:						
Grade 1	33	10	4	47	44 (97.9%)	1 (2.1%)
Grade 2	16	11	2	29	27 (93.1%)	2 (6.2%)
Grade 3	3	1	2	6	5 (83.3%)	0 (0.0%)
Grade 4	0	1	0	1	0 (0.0%)	1 (100.0%)
Totals	52	23	8	83	76 (91.6%)	4 (4.8%)
Mixed	8	3	1	12	11 (91.7%)	2 (16.7%)
Basal cell	35	30	6	71	64 (90.1%)	0 (0.0%)
Totals	95	56	15	166	151 (90.9%)	6
Cures	92 (96.8%)	49 (87.5%)	10 (66.7%)	151 (90.9%)		
Metastases*	1 (1.7%)	4 (15.4%)	1 (11.1%)	6 (6.3%)	1 (16.7%)	

*Exclusive of basal-cell lesions.

STAGE OF DISEASE, DURATION AND SIZE

The mean duration before treatment was ten months. The average size of the lesion at the time of treatment was 16 mm. For purposes of analysis the lesions were further classified according to three stages of extent (Table 3). Ninety-five were less than 15 mm. in size and clinically did not exhibit fixation to the underlying cartilage. These were considered localized (Stage 1). There were 56 lesions between 15 and 30 mm. in size, with clinical fixation to cartilage. These were regarded as exhibiting invasiveness (Stage 2). Fifteen lesions were greater than 30 mm. in size, involved multiple areas of the pinna or actually invaded cartilage. These were believed to be advanced (Stage 3). Three Stage 1 lesions were considered local failures, as were 3 Stage 2 and 4 Stage 3 lesions. Four failures were due to metastasis in Stage 2, and 1 to metastasis in Stage 3.

SITE OF ORIGIN

Certain specific sites of origin that presented similar problems in treatment were grouped together (Fig. 1). Site A consisted of 23 lesions originating in the concha, Site B of 22 originating along the anterior base of the pinna (crus of helix, tragus, intertragal area, antitragus and lobule), Site C of 76 of the rim of the pinna (helix and anthelix), and Site D of 45 of the posterior surface of the external ear and auriculomastoid sulcus. Lesions of the external auditory canal were not included in this survey because of their well known differences in pathology and clinical behavior. Basal cell carcinomas predominated on the posterior surface of the ear; elsewhere, epidermoid carcinomas were more common.

The more central lesions (Sites A and B) tended to be more advanced, and to have higher rates of metastasis, recurrence and ultimate failure (Table 4). There were 12 failures among the 45 lesions in Sites A and B, as compared with 5 among the 121 lesions in Sites C and D.

SECONDARY CASES

In the same period 25 lesions unsuccessfully treated elsewhere were seen (Table 5). This group comprised 16 three-year cures, including 2 patients whose metastases were extirpated by regional-lymph-node dissec-

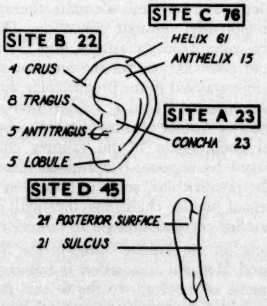

FIGURE 1. *Four Sites of Origin of Carcinomas of the Pinna.*

tion, and 9 failures, of which 3 were due to metastases and 6 to local recurrences. Table 5 shows the distribution according to stage and site of origin. Nineteen lesions were treated primarily by surgery. Seventeen were cured locally, although 2 of these were considered failures after unsuccessful irradiation of regional metastases. Six were treated, initially, by irradiation, and of these, 5 were local failures. Thirteen lesions were epidermoid carcinomas—7 Grade 1, 3 Grade 2, 2 Grade 3, and 1 Grade 4. There were 11 basal-cell lesions, and 1 basosquamous carcinoma.

Discussion

The interpretation of the information outlined above will be of most benefit if emphasis is placed on analysis of the failures. Of the 15 failures in the primary cases after three years, 4 were due to metastases alone, and 11 to local recurrences.

None of the patients with failures because of metastases alone had received adequate therapy in the form of regional-lymph-node dissection. There were no cases of widespread metastases, and the nodes involved were few. Lesions on the anterior surface of the pinna metastasized to the preauricular, subparotid, and upper internal jugular lymph nodes. Those on the posterior surface also involved the upper lateral cervical chain. Most of the failures could have been salvaged by regional-lymph-node dissection including the preauricular, subparotid and at least the upper internal jugular chain, together with dissection of the posterior cervical triangle in posterior lesions.

At present, in the Tumor Clinic of the Massachusetts General Hospital irradiation is not regarded as the treatment of choice. In the 6 local failures, in which the initial therapy was irradiation, the treatment is considered to have been inadequate. Not only are low dosages of radium or x-rays (as in several earlier cases) without value but also adequate dosages which probably occurs subcutaneously along both surfaces of the external auditory meatus, deeply into the external auditory canal and into the parotid gland, is not easily detected clinically, and may not be identified at operation. Even if they recognize this extension most surgeons may rightly be hesitant to undertake, under local anesthesia, the major maneuvers necessary in dealing with these structures, or may not feel familiar with this type of surgery, with the result that excision may be inadequate. Lesions of the concha and of the anterior base of the pinna should therefore be handled with close attention to the possibility of concealed spread. Operation should be carefully planned, with recognition of the possible need for general anesthesia and for dealing with the surgical problems concerning the external auditory canal and the parotid gland—namely, the partial ablation of these structures.

Table 4. *Site of Origin, Pathology, Stage and Result after Three Years.*

Factor	Site A	Site B	Site C	Site D
	no. of cases	no. of cases	no. of cases	no. of cases
Type of lesion:				
Epidermoid	12	11	45	15
Mixed	1	1	9	1
Basal cell	10	10	22	29
Totals	23	22	76	45
Stage				
1	7	10	53	25
2	9	8	21	18
3	7	4	2	2
Totals	23	22	76	45
Cures	18 (78.3%)	16 (72.7%)	75 (98.7%)	42 (93.3%)
Metastases*	2 (15.4%)	2 (16.7%)	1 (1.9%)	1 (6.3%)†

*Exclusive of basal-cell lesions.
†Patient cured.

Conclusions

Skin cancer of the pinna is principally a disease of elderly men who have had considerable exposure to sun and weather.

Surgery is the treatment of choice for the local lesion, for any local recurrences and for any suspected regional metastases.

Lesions involving the concha and anterior base of the pinna warrant especial care in evaluation and treatment.

The reported rates of three-year and five-year cures in this disease seem unnecessarily low.

223 Thayer Street

TABLE 5. *Sites of Origin of Secondary Lesions, with Stage and Three-Year Results.*

STATUS OF LESION	SITE A	SITE B	SITE C	SITE D	TOTALS	CURES
	NO. OF CASES	NO. OF CASES	NO. OF CASES	NO. OF CASES		
Stage 1	0	1	1	2	4	4(100.0%)
Stage 2	2	0	4	4	10	8(80.0%)
Stage 3	2	7	1	1	11	4(36.4%)
Totals	4	8	6	7	25	16(64.0%)
Cure	1(25.0%)	3(37.5%)	5(83.3%)	7(100.0%)	16(64.0%)	
Metastasis*	2(33.3%)	0(0.0%)	1(25.0%)	1(20.0%)	4(28.6%)	2(50.0%)

*Exclusive of basal-cell lesions.

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VOLVULUS OF THE GALL BLADDER ASSOCIATED WITH ACUTE MYOCARDIAL INFARCTION*

Report of a Case and Review of the Literature

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VOLVULUS of the gall bladder is rare enough to be noteworthy. Owing to the diagnostic difficulties presented when it was associated with acute myocardial infarction, we consider the following case of general interest.

CASE REPORT

Mrs. M. M. (N.-W.H. 53-8390), a 79-year-old widow, was admitted to the hospital with the chief complaints of vomiting, pain in the anterior aspect of the chest and right-upper-quadrant pain of about 6 hours' duration.

The history of the present illness dated back many years. She had placed herself on severe dietary restrictions because most foods caused eructation and severe indigestion, for which she obtained some relief by taking a large amount of alkali. She had had similar right-upper-quadrant pain on a few occasions in the past 5 or 6 months, but there had been no vomiting. These episodes had not been relieved by alkali. She had never noticed jaundice or acholic stools. An alcoholic intake was denied.

She stated that she had suffered from heart trouble for years. The symptoms elicited comprised precordial chest pain and a chronic cough but no ankle edema, orthopnea, palpitation, dyspnea or classic anginal radiation of pain. The chest pain, however, was relieved by nitroglycerin. There was no history of rheumatic fever.

The family history was of interest in that the patient's mother had apparently died of gall-bladder disease.

Physical examination revealed an acutely ill woman who was oriented and co-operative. The skin was pale but not icteric or cyanotic. The chest was clear to percussion and auscultation, and the heart was not clinically enlarged. There was a regular rhythm; no murmur or thrill was present. The abdomen was protuberant. The liver and spleen were not palpable, and only 1 observer palpated a mass in the right upper quadrant. There was acute tenderness and guarding on palpation over the entire abdomen but much more so, with associated spasm, in the right upper quadrant, where rebound pain was referred. Peristalsis was normal. Rectal examination was negative.

The temperature was 97°F. by mouth, the pulse 80, and the respirations 20. The blood pressure was 180/70.

The urine was cloudy yellow, with a specific gravity of 1.022, pH of 4.5, a + + test for albumin and a + + + + test for sugar (during an infusion of 5 per cent dextrose in water) but a negative test for acetone; the sediment contained 0-1 white cells per high-power field, with no red cells. The sample was crowded with bacteria. Examination of the blood disclosed a hemoglobin of 12.1 gm. per 100 cc., a hematocrit of 40 per cent and a white-cell count of 7400, with 87 per cent neutrophils, 13 per cent lymphocytes and normal platelets and morphology. The icteric index was 6 units. The serum bilirubin was 0.2 mg. per 100 cc., direct, 0.3 mg. per 100 cc. indirect, and 0.1 mg. per 100 cc.,

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prompt. The carbon dioxide was 23.5 milliequiv. per liter.

A plain film of the abdomen and a chest film were normal.

An electrocardiogram was reported as probably abnormal and suggestive of an early or fresh myocardial infarction. There were small Q waves in Leads 1, aVL and V_3 to V_6 (variable in Lead V_3), with ST-segment elevation in the same leads. There was a tiny R wave in Lead V_2.

The initial diagnosis was acute cholecystitis and probably angina pectoris due to hypertensive arteriosclerotic heart disease. Because of the absence of satisfactory evidence of an acute inflammatory process and since the patient was afebrile considerable weight was placed on the suggestive electrocardiographic findings. She was given sedatives and penicillin in the hope that the diagnosis would define itself. Her condition was unchanged on the day of admission, and that night the white-cell count was only 11,400, with 90 per cent neutrophils, 9 per cent lymphocytes and 1 per cent monocytes. She remained afebrile.

On the morning of the day after admission the white-cell count had risen to 13,200, with 86 per cent neutrophils and 14 per cent lymphocytes. She continued afebrile, and an electrocardiogram demonstrated a progression of the electric changes suggestive of an acute anterior myocardial infarction. There were deeply inverted T waves in Leads 1, 2, aVL, and V_4 to V_6. The abdominal findings on physical examination remained unchanged. There were no signs of congestion on auscultation of the chest. Until about 5 p.m. the patient's condition was static. Laboratory examination in addition showed a serum amylase under 80 units per 100 cc., a prothrombin time of 100 per cent and a nonprotein nitrogen of 29 mg. and a fasting blood sugar of 120 mg. per 100 cc. In the early evening of that day, however, she became acutely disoriented and stuporous, and the abdomen was more protuberant. Bowel sounds were absent. The only response was that of wincing on palpation of the right upper quadrant. X-ray examination at that time revealed only minor congestive changes in the lung fields. The abdominal film remained normal. The white-cell count was 11,700, with 89 per cent neutrophils, 10 per cent lymphocytes and 1 per cent monocytes.

The possibility of 2 concurrent diseases could no longer be ignored. In view of the acute change perforation of the gall bladder and an associated chemical peritonitis were considered possible. The patient was taken to the operating room for a proposed cholecystostomy under local anesthesia.

When the peritoneum was opened a globular, purple-black mass about 7.0 cm. in diameter was found twisted into the wound in a clockwise manner for about 180°. The mass was a gall bladder twisted and anchored only at the liver edge, its normal position in the liver bed being occupied by a long cystic duct, which extended from the twist at the liver edge to the common duct. No stones were palpated in the cystic or common duct, neither of which was dilated. The gall bladder was simply amputated at the liver edge, and a straight urethral catheter sewn into the cystic duct for drainage. A cigarette drain was placed in Morrison's pouch for drainage at the angle of the wound. The abdomen was closed in layers.

After operation chlortetracycline was given intravenously, and administration continued daily thereafter. The patient was maintained on oxygen and intravenous infusions of fluids. Her comatose condition remained unchanged.

An electrocardiogram on the day after operation showed striking changes, which were confined to the chest leads. The R waves were absent in Leads V_1 and V_2 and tiny in Leads V_3 and V_4. The QRS complex in Lead V_4 was M-shaped. The ST segment was elevated in Leads V_2 to V_6, and the deeply inverted T waves of the previous tracing had become diphasic, possibly owing to electrode placing. A day later, on the evening before death, the tracings demonstrated further changes. The ST segment had become slightly elevated in Leads aVL, V_5, V_4 and V_2. The T waves had changed to upright in Leads 1 and aVL but low in Leads 3 and aVF. There were no changes in the R waves of the chest leads.

The patient's condition deteriorated rapidly. The pulse became thready, weak and irregular. Despite stimulants and nor-epinephrine she died in the early hours of the 5th day in the hospital.

The pathological diagnosis of the surgical specimen was infarct necrosis of the gall bladder and chronic cholecystitis. No stones were present. The significant findings of the post-mortem examination were limited to the heart and lungs. There was a massive infarction of the left anterior myocardial wall and changes of congestive heart failure in the lungs.

Review of the Literature

Volvulus or torsion of the gall bladder has been recognized since 1898, when Wendel[1] described the first case. Since then there have been many reports. In 1934 Short and Paul[2] described the condition and seemingly defined it as a clinical entity. Gross,[3] in 1936, discussed the anomalies of the gall bladder and reviewed 50 cases of torsion occurring between 1908 and 1933. Nine years later Leger et al.[4] collected 91 cases and added 3 of their own. Husband and Schmitt,[5] in the same year, listed 80 cases chronologically. Most of the earlier descriptions appeared in the foreign literature. These lists do not entirely overlap. We have collected 28 reports since 1945, making the total number of cases reported approach 130.

The disease is certainly not a clear-cut entity and has only been diagnosed at the time of operation for an acute condition of the abdomen.

The age of patients has varied from five (Cuervo's patient, referred to by Leger et al.[4]) to ninety-three years,[6] the ratio of females to males being about 3:1. The age group most often affected is that over sixty. There may not be a previous history consistent with cholecystopathy. When one has decided that the patient has a surgical condition of the abdomen the diagnosis of acute gall-bladder disease is likely to be obscured by the fact that the appearance is not that of the typical "gall-bladder prototype." Throughout the literature patients are described as visceroptotic and asthenic. The onset of symptoms is usually acute and unheralded. The patient is not typically "toxic" but is in acute distress. Jaundice is the exception. The abdomen varies from boardlike to soft. Ileus is not common. The finding of a mass, which is not the rule, has been reported in the right upper quadrant, in the right flank[7] or over the pelvic brim.[8,9] The patients do not usually have stones visible on x-ray study or in the specimen. There is no hyperpyrexia, and the white-cell count is not excessively high. In the case reported above, it did not vary appreciably.

The various preoperative diagnoses have been acute and subacute cholecystitis,[10] empyema of the gall bladder,[11] perforated peptic ulcer,[6,12,13] obstructing tumor of the intestine,[4] retroperitoneal tumor,[9] twisted ovarian cyst[8] and appendicitis[14-16] or appendiceal abscess.[4] A further complication in the diagnosis before operation is reported in a case of coexisting acute appendicitis[5]; acute myocardial infarction was present in the case reported above.

Perforation had only been mentioned in 2 accounts up to 1945,[5] and none had described large omental masses or dense adhesions about the gall bladder, as one might expect if the process had been associated with typical acute cholecystitis. Therefore, all the cases can apparently be immediately remedied by cholecys-

tectomy, which is indeed only an amputation of a free-floating vesicle in most cases.

The mechanism of the twist has been given attention. If it is clockwise it is thought to be due to the motion of the pylorus and duodenum, and, if it is counterclockwise, to peristalsis of the transverse colon.[2,17] In either event volvulus cannot occur unless the vesicle is suspended from the liver edge, from the gall-bladder bed by a long mesentery or from the common duct; all these situations have been described. Short and Paul[2] also note the possibility of torsion of only the distal portion of the gall bladder, which may hang free and twist to form an hourglass. They mention 3 cases. Torsion of one limb of a Y-shaped, double gall bladder has been reported.[18]

Gross[5] believes that the reason the volvulus does not cause symptoms sooner in life may be the disappearance of the supporting fat from the surrounding viscera with age. Atrophy of the tissues allows greater ptosis, and the possibility of torsion is enhanced.

Of the 21 cases in 18 reports reviewed, which were among the 28 articles that have appeared since 1944, there were 14 females and 7 males. Among the cases were those of Forty,[19] Haines and Kane,[20] St. John and Burns[21] and Lind.[22] Fifteen patients recovered; 3 died, and the fate of the remaining 3 is not recorded. Cholelithiasis was present in 8, absent in 9 and not mentioned in 4. The average age was sixty-nine years. A mortality of about 16 per cent is the figure usually cited.

The cardiac problem is, of course, not related to the congenital anomaly permitting torsion, but the relation between anginal symptoms and abdominal complaints certainly caused our confusion. In a paper on cardiac improvement after gall-bladder surgery Fitz-Hugh and Wolferth[23] make the pertinent remark that "an attack of angina pectoris or acute coronary occlusion may so closely mimic acute calcareous obstruction of the biliary tract, or some other more surgically imperative catastrophe in this region, that the surgeon may be disastrously tricked into operating." On the other hand Barker et al.[24] point up the reverse of the same problem: they present 2 cases of gall-bladder disease and 1 of perforated peptic ulcer that had erroneously been called coronary-artery disease.

SUMMARY

A case of volvulus of the gall bladder in association with acute myocardial infarction is reported.

The diagnostic problems are considered, and a review of the available literature since 1945 is presented.

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MEDICAL PROGRESS

MYASTHENIA GRAVIS

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A REVIEW of myasthenia gravis was published in the *Journal*[1] in 1951, to bring the survey of the published reports up to the midyear. The present paper continues the survey of the subject to the close of 1953, for the most part covering a period of about two and a half years. Although practically every paper printed during that time has been scrutinized, only part of the literature is included in the references here discussed. Papers of minor interest, single case reports of minimal value and a few reviews have been omitted. It is hoped that no paper of importance has been missed. A few technical essays were purposely omitted, as not coming within the scope of the review, which is primarily aimed to cover the clinical

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progress of knowledge of the disease as recorded in the current medical literature.

Childhood and Infancy

The disease is now recognized as occurring in infancy and childhood. Wyllie and his associates[2] described 4 patients with the first symptoms occurring between three and a half and ten years. The first child, aged three years and eight months, had symptoms within six weeks of an attack of tonsillitis. Remission without treatment was followed by relapse in an intermittent manner over a period of five years, when the diagnosis was first made and neostigmine given by mouth. Six months later she survived an attack of pneumonia and subsequently had a remission, only to relapse in a year and die of respiratory failure. Seven years of observation and treatment, with 7 hospital admissions during this period, did not suffice to save this patient's life. This is a good example of the severe type of myasthenia gravis, progressing by remission and relapse, difficult to control and with a grave prognosis. Would thymectomy have been helpful? At autopsy the thymus was "normal," without germinal centers, but such an appearance does not preclude the possibility of provoking a remission by surgical removal.

Three of the 4 patients discussed by Wyllie, Bodian and Burrows[2] were operated on for the removal of the thymus. There were no immediate deaths, but 1 child died in a sudden relapse after a stormy convalescence four months after operation. In this patient the gland removed at operation showed no involution but did exhibit medullary foci simulating germinal centers. At autopsy further thymus tissue was found, showing obliteration of the corticomedullary pattern. This was thought to represent rapid regeneration of hyperplastic glandular tissue four months after partial thymectomy, and possibly to indicate also that the thymic changes were secondary to myasthenia. In contrast the thymus glands removed at autopsy from an unselected series of 100 children showed involutionary changes of varying degrees in more than 80 per cent. Lymphoid hyperplasia without germinal-center formation was found in only 5 per cent. Of the other 2 children on whom thymectomy was performed 1 was in good health six years after operation, maintained on 15 to 30 mg. of neostigmine by mouth daily. The other child was free from symptoms one year after operation.

Congenital Myasthenia Gravis

Mackay[3] reported on a patient, the firstborn of binovular twin girls as the result of the first pregnancy of a nonmyasthenic mother. The second child was normal, but the first had difficulty in feeding from infancy. Ptosis, diplopia, facial weakness and other symptoms developed but so slowly that the diagnosis was not made definitely until the patient was over seven years of age. The response to the Viets–Schwab diagnostic test was positive. The child was well maintained on 12 mg. of neostigmine bromide (not methyl sulfate) by mouth a day. This is the fourth case reported, the previous cases having been noted in 1951.[1]

A fifth patient, described by Walker,[4] was a girl two months old, born of a nonmyasthenic mother. The patient responded rapidly to neostigmine and was finally regulated on 7.5 mg. every eight hours. This proved to be excessive and was modified to 5 mg. At eight months the child was getting along fairly well. If she does not do well radiation, possibly followed by thymectomy, should be given consideration.

Neonatal or Transitory Myasthenia

McKeever[5] reports another case of transitory myasthenia in a child born of a myasthenic mother. Symptoms were not noted at birth but were well marked at the end of twenty-two hours. The response to neostigmine was prompt, and medication was discontinued at the end of fifteen days. The child was well at four months. The author states that no case of myasthenia gravis in infancy had been observed before the introduction of neostigmine in 1934. Keynes[6] found only 1 case of transitory myasthenia in 27 newborn children, the infant becoming normal in four weeks; 25 were normal babies, including 1 pair of twins. One pregnancy terminated in a miscarriage. Gans and Forsdick[7] added the thirteenth case to be reported. They believe that "infants showing transient neonatal myasthenia are essentially normal, that they receive a curare-like substance from their myasthenic mothers via a defective placenta, and that their myasthenia disappears, never to return, when this substance has been destroyed." With this point of view most observers are now in accord, the practical point being that, without immediate recognition at birth, the newborn infant, if not treated with neostigmine promptly, may die. A similar case was presented by Kilbrick.[8] Some infants may survive with only small doses of neostigmine, if provided with expert nursing care as in the case reported by LeRiche and Rosevear.[9]

Diagnosis

Dundee and Gray[10] found evidence that patients with myasthenia are sensitive to *d*-tubocurarine chloride and gallamine triethiodide by "competition block" at the motor end-plate, while decamethonium, on the other hand, acts in the same region by depolarization. Respiration was completely stopped by 0.5 mg. of *d*-tubocurarine chloride in a myasthenic patient awaiting thymectomy. Voluntary respiration could not be carried out until the patient was revived by 1.3 mg. of atropine and 5.0 mg. of neostigmine. Nine days after thymectomy respiration was only slightly depressed by the same dose of *d*-tubocurarine, and the response to neostigmine and atropine was minimal. The respiratory changes noted after the use of decamethonium in doses of 0.1 to 0.5 mg. were within the limits of normality.

The test, a valid one although somewhat dangerous to carry out, is of considerable use in estimating the response to thymectomy, but usually the patient quickly senses improvement when it occurs, and promptly dispenses with neostigmine. If there is any doubt about the diagnosis before operation tests of this type, when indicated, are justified. The slight or negative effect of decamethonium may be due, as noted by Churchill-Davidson and Richardson,[11] either to the destruction of the compound before it is able to act on the muscle fibers or to an inherent resistance of the end-plate of myasthenic muscle fibers to its action. The drug appears to have little value in either diagnosis or treatment of myasthenia gravis.

Of somewhat more practical value in diagnosis is the response to edrophonium chloride (Tensilon) as evaluated by Osserman and Kaplan.[12] By intravenous injection 10 mg. (1 cc.) of the drug was given. If a decisive result was not obtained after thirty to sixty minutes the test was repeated with 15 to 20 mg. The response was rapid and usually complete, lasting five to thirty minutes. There were no hazardous or uncomfortable side effects. Similar results were reported by Westerberg, Magee and Shideman[13] in a prior publication. The chief value of Tensilon as a diagnostic agent may rest on its effect in myasthenia gravis regardless of the presence or absence of premedication with atropine, neostigmine, tetraethyl pyrophosphate, ephedrine or potassium salts.

The intra-arterial injection of neostigmine as a diagnostic test has been recommended in the past, and the method has even found its way into textbooks. Hutchinson and Matthews[14] observed that when a dose of 1.0 mg. to 1.5 mg. was injected in patients who had muscular weakness of the arm on the same side as the brachial artery used for the test, the increase in grip was rapid. In patients whose muscular weakness was not in the injected arm the strength of grip was greatly reduced, and the muscles below the point of injection went into course fasciculation. These changes never occurred in the muscles that were affected by the disease. It was believed that the test was of value only under these restricted conditions, and, therefore, intra-arterial injection as a diagnostic procedure appeared to be of extremely limited value.

Botelho, Deaterly and Comroe[15] took electromyograms of the orbicularis oculi muscle, using the apparatus of Harvey and Masland (1941), in 4 patients and found a progressive decrease in amplitude of successive summated action potentials on repetitive stimulation of the motor nerve. These observations confirm the impression that the facial muscles are involved early in the disease and frequently more severely than most other muscle groups. Although requiring an elaborate technic the test is most reliable in making an early and positive diagnosis. It cannot, however, be used clinically except under exceptional conditions.

Thymic Tumors and Their Location

Benign Tumors

Fulghum[16] reported the removal of a large, benign, congenital, cystic tumor from the anterior mediastinum in a man in whom symptoms of myasthenia had developed in about four months at the age of fifty-six. The exact origin of the cyst could not be stated, but it was not dissimilar to the tumor of the thymus found in Blalock's original case in 1939. The patient had not received radiation before operation. The relation of tumors of this type to myasthenia is not clear. The postoperative remission, which was prompt and complete, could, according to the author, have been coincidental. According to a personal report from the author there was no recurrence of the tumor over six years after operation, but the myasthenia had gradually increased.

Ringertz[17] examined the thymus glands in 27 cases, 9 being those of patients surviving thymectomy, 10 patients who died after thymectomy, and 8 post-mortem cases. Thymomas were found in 9 cases, hyperplasia in 3, and retarded involution in 9; 6 appeared normal. Other endocrine glands, except the thyroid, did not present any obvious abnormalities: 5 cases gave evidence of pathological changes in the thyroid gland. Lymphorrhages were found in skeletal muscles in nearly two thirds of the 27 cases examined. As in the series described by Castleman and Norris little agreement emerged between the thymic status and the duration and severity of the disease. The disease, however, was most progressive in a group of young patients with hyperplastic thymus and on the average most tardy in the cases with high-grade involution. The material collected from three hospitals in Sweden is clearly presented, with tables giving the clinical course of all cases. The author points out the difficulty in correlating the changes in the thymus with the clinical state of myasthenia gravis. In his series nearly 80 per cent of the cases of myasthenia gravis showed thymic alteration, but other cases, some of longstanding and severe myasthenia, demonstrated no morphologic thymus change. Thymic alterations may occur, moreover, independently of the disease, and true thymoma, not associated with myasthenia, has frequently been reported. Although other endocrine structures do not appear to be involved, the thyroid changes found by Ringertz (nodular goiter, Graves disease or lymphadenoid goiter) indicated a reciprocal hormonal influence between the two glands.

Malignant Thymomas

Cases with local extensions and metastases confined to the limits of the thoracic cage continue to be reported. Levine,[18] Thévenard and his associates,[19] and Derow, Schlesinger and Persky[20] report tumors of this type. Fershtand and Shaw[21] observed a patient, twenty-seven years of age, without signs of myasthenia but with a mediastinal mass as disclosed by x-ray examination. At operation a large, calcified tumor was found,

which could not be entirely removed. It proved to be a malignant thymoma. On the second postoperative day, the patient gave signs of myasthenia, controlled by neostigmine, only to survive the operation for eighteen months, dying of cardiac failure. The pericardium was replaced by a tumor, which had invaded the wall of the ventricle. The value of early and complete removal of tumors of the thymus is emphasized in view of the fatal course pursued by tumors of this type.

Thymomas may be located ectopically as in the case encountered by McBurney, Clagett and McDonald.[22] Grossly and histologically identical with thymoma, the tumor was found in the parenchyma of the right middle lobe of the lung and was successfully removed. The patient, a woman sixty-five years of age, had had symptoms of myasthenia for only a few months. No tumor was found in the anterior mediastinum, either at operation or at autopsy two months later. The authors believe that, in patients with myasthenia undergoing a negative exploration of the mediastinum, the possibility of ectopic tumors should be kept in mind. This case should be contrasted with that reported by Derow, Schlesinger and Persky,[20] in which the intrapulmonary thymoma appears to have been secondary to a primary tumor arising in the thymus.

Intrapleural Thymus

The thymus, although usually situated in the anterior mediastinum, may descend into the intrapleural space. A tumor in this area was discovered by Peller and Barrie[23] in a forty-six-year-old man who had had symptoms of myasthenia only three months. He died suddenly. At autopsy the tumor, consisting of a uniform, benign hyperplasia only, lay in the right pleural cavity suspended from the superior mediastinum by a tubular reflection of parietal pleura.

Results of Thymectomy

Ross[24] analyzed the results of thymectomy in 100 consecutive patients operated on by Keynes, omitting all patients with thymoma. Seven patients had died, 1 of myasthenia gravis, leaving 93 for evaluation. The average postoperative period was four and a half years. Forty-one patients needed no treatment at the time of evaluation, being in complete remission; 26 had slight or inconstant symptoms and were able to work without limitations. Thus, 67 patients, omitting those with thymic tumors, were markedly benefited by the operation. Another 20 patients were less favorably affected, although slightly improved; 6 were unchanged or worse. The age at onset of the myasthenia did not appear to be a significant factor in the results, but patients who had had the disease for the shortest time before operation showed the most improvement. Seen by three observers, who expressed unanimous opinions, the patients were graded A, B, C and D, A indicating complete remission. Of the 100 patients 73 were female, and 27 male. The mean age at onset was thirty-one years, and ages ranged from the first to the sixth decade. In Group A (those that benefited most) the mean preoperative duration was only two and a half years; in B, C and D, the durations were seven years or more. These statistics, carefully compiled, present a strong argument for thymectomy. The figures were compared with equivalent percentages from 3 series of patients treated by medical means alone; Classes A and B were smaller, and the proportion of deaths from myasthenia gravis was much higher than that in the thymectomized patients.

Brea and his associates[25] in Buenos Aires reported on the results of 24 thymectomies, 20 in females and 4 in males, the patients ranging in age from thirteen to sixty years. Two patients died, an operative mortality of 8.3 per cent, or about the same average as in other series. Three patients had thymomas. Eighteen of 19 who could be evaluated showed excellent or good remissions. This is one of the best series so far reported, with a high degree of recovery, including 7 patients in complete remission. The majority of the patients were examined by Goñi, and others by Lanari.

Schwab and Leland,[26] using the 78 patients operated on at the Massachusetts General Hospital and incorporating those described by Viets in 1950 and by Schwab and Passouant[27] in 1952, found 63 per cent of the females but only 24 per cent of the males either in complete remission or significantly improved. The opposite was true in the cases treated medically: 34 per cent of the females but 56 per cent of the males were in the AB group. Patients with thymomas were, with a few exceptions, not benefited by the operation. Females under thirty years of age responded best to thymectomy, and in this group, if thymoma was not present, the expectation of a provoked remission was fulfilled. In men over thirty the operation appeared to be contraindicated, but the group of 25 cases was considered too small to warrant dogmatic conclusions.

Grob[28] reported 44 cases of thymectomy in his clinic of 202 patients. There were 19 males and 25 females, subjected to the operation two to twelve (average of six) years before evaluation. About a third were operated on during the first year of the illness. Their average age was thirty-three. Approximately the same proportion of patients died in each group, those operated on and those who were not, and the proportion of patients who had remissions was also similar. The course of the patients who had thymectomy was in general only slightly better than that of those who survived without operation. In 40 patients who had irradiation treatment, the degree of improvement was only slightly greater than that in 118 patients who were treated by medical therapy alone. Of 15 patients with thymoma 10 had a rapid, fulminating course terminating in death, regardless of thymectomy.

This series contains the first cases in which thymectomy was performed by Blalock twelve years ago.

The average age at operation was considerably higher (thirty-three years) than that of later series. The death rate was also high (35 per cent) but not higher than that in the patients not operated on. The number of immediate or postoperative deaths is not given, so they cannot be eliminated from the general death rate from the disease.

Dunlop,[29] in a thoughtful study, reviewed the response to the operation in 19 cases. The results were in close agreement with the reports of Blalock, Eaton, Harvey and Viets, but were much less favorable than those in the 100 patients operated on by Keynes and evaluated by Ross.[24] When the four series reported from America were added to those of Dunlop 132 cases were available for comparison with 100 in the Ross compilation. Keynes and Ross found 67 per cent of their patients in complete remission or considerably improved (AB), whereas the combined figures of the others could record only 40 per cent in these classes. Dunlop suggests that the difference lies, at least in part, in the fact that Keynes has been more radical than the others, and has included a larger portion of mild cases. Dunlop found that the early and sustained improvement shown by some patients made it difficult to escape the conclusion that thymectomy was instrumental in causing the alteration in their clinical state. He also believed that patients with thymomas should be operated on although the prognosis might not be good.

Statistics

Schwab and Leland[26] first determined the age at onset in 367 patients; the disease began before thirty-one years in 62 per cent of the females and in only 27 per cent of the males. In females the mean age at onset was twenty-one to twenty-five years; in males it was sixty-one years or over. Thus, it was not surprising that 53 of their 78 patients subjected to thymectomy were female, as commonly reported in other series. These were matched by sex, age at onset, severity of the disease and presence or absence of thymoma, all factors in determining the results of thymectomy, with an equal number of patients from those not operated on. The category of complete remission and significant improvement (AB) contained 63 per cent of the females but only 24 per cent of the males—a striking difference in the response to thymectomy. In a control group the results were almost the exact opposite—34 per cent of the females and 56 per cent of the males were considered as in the AB range (Fig. 1).

Grob[28] used the records of 118 patients who were not operated on for comparison with 44 who were. The number of deaths, both immediately after operation and subsequently, was nearly the same, but the patients with thymectomy achieved a somewhat higher AB classification (43 per cent as compared with 32 per cent) than those receiving medical treatment only.

From the statistics at hand, therefore, with all cases considered the advantages of thymectomy are slight. It is only when sex and age are given primary consideration, as in the report of Schwab and Leland, that the operation can be fully evaluated. When the thymus gland is removed for myasthenia gravis in females under thirty years of age remission or significant improvement may be expected in over 60 per cent. All other patients appear to do better in general on medical treatment. The number of cases analyzed,

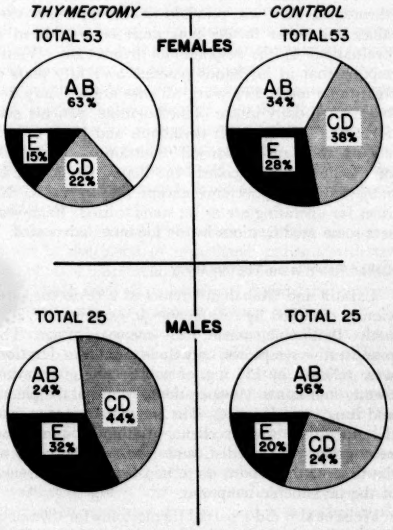

FIGURE 1. *Analysis of the Effect of Thymectomy (Reproduced from Schwab and Leland[26] with the Permission of the Publishers).*

however, is not large enough for one to draw categorical conclusions; only trends can be noted until the total cases reach 1000 or more. The influence of age, duration of disease, length of time under medical treatment before operation, presence of thymoma, effects, if any, of irradiation and variations in the progress of the disease are of uncertain significance at present. The importance of the consideration of sex is now somewhat clearer than it was a few years ago, but even that factor requires more study before a sound treatment policy regarding thymectomy can be laid down.

Still other questions are unanswered. Why do patients with thymoma respond so poorly to its removal? Why do some patients with only moderate hyperplasia of the gland and considerable involution sometimes have a complete remission after thymectomy? Why are some remissions delayed until the second or third

postoperative year? Why are the remission rates much higher in some reported series than in others? Although these fundamental problems are not as yet resolved, most clinicians believe the operation to be of value in selected cases. How to select these cases is only slowly being disclosed.

Generalized statistics of the total number of cases in which operation is performed have almost lost their value. The problem has become one of "on whom, for what and when." Patients with thymomas in general react to operation quite differently from those without thymomas. Age, sex, previous treatment, course variables and other factors now must be considered in evaluations of the response to thymectomy. Viets[30] reports that in his hands patients over fifty years of age, those under five years, all who are well adjusted on a small daily intake of neostigmine, patients over forty years of age with thymomas and those experiencing good and prolonged remissions in the course of the disease, particularly the males, should not be subjected to thymectomy except in rare cases. No rules for operating are as yet standardized. Each year sees some modifications in the measures advocated.

Other Reports on Thymectomy

Lazatin and Manahan[31] removed a thymoma, previously disclosed by roentgenologic examination, in a native Philippine woman, forty-one years of age. The preoperative symptoms, only three months in duration, were relieved by 135 mg. of neostigmine given every twenty-four hours. At operation portions of the pleura and lung were invaded. The immediate response to the operation was excellent. Within a month no neostigmine was needed, and four months later, at the time of the report, there had been no recurrence of the myasthenic symptoms.

Weiss et al.[32] did a partial thymectomy for thymoma on a twenty-two-year-old woman who had been ill for three months after a pregnancy. There was immediate improvement, followed by relapse. Removal of the rest of the thymus at a second operation was followed by an excellent remission.

Sellors[33] operated on 37 patients, 5 without myasthenic symptoms. There was 1 postoperative death, and 2 patients died subsequently. All patients showed some improvement, but the degree was not assessed. Four out of 5 patients with benign tumors did well. The author believed that the results warranted the conclusion that thymectomy offered better hope of permanent relief than medical treatment, particularly if carried out in the early stage of the disease.

Bergh[34] operated on 12 patients, with 4 postoperative deaths. Ten were female, and 2 male; the ages varied from seventeen to fifty-one. Two had thymomas. Of 8 living patients 7 were considered improved in a follow-up period of two and a half to six years, but in only 2 of the 7 could he attribute the gain to the removal of the thymus.

The series, though small, is carefully reported. The 4 postoperative deaths occurred within two weeks. Autopsies are carefully set forth, with the usual findings of bronchial block by mucus or purulent secretions, atelectasis and bronchopneumonia. Bergh noted that in patients whose vital capacity was low (1000 cc. or less), and in the event that this rate could not be increased to more than 1400 to 1800 cc. by neostigmine treatment before operation, the respiratory margin was so narrow that it constituted a strong factor in a decision to postpone thymectomy or even to give up the operation entirely.

Brown,[35] who operated on most of the patients described by Dunlop,[29] attempted to remove the thymus in 1 patient whose condition was rapidly deteriorating in spite of increasing amounts of neostigmine. As others have learned under similar circumstances, the patient survived the operation for only a few hours. In 2 patients who died Brown found no thymic tissue at autopsy. He therefore doubted if the poor results could have been due to incomplete removal of the thymus. Other investigators have reached similar conclusions.

X-Ray Diagnosis and Treatment of Thymoma

Harper[36] found that approximately 13 per cent of patients with myasthenia gravis have thymomas. The shadows are easily overlooked without careful screening and unless tomography is carried out. Although nonmyasthenic tumors occur a lesion in the anterior mediastinum in a myasthenic patient is almost certainly thymic in origin. Many examples of spherical, lobulated and plaque tumors are reported in Harper's series. The conclusions reached by Harper have been confirmed in other clinics, but many radiologists fail to search with sufficient care for these elusive growths. The finding of a thymoma in a nonmyasthenic patient does not preclude the possibility that myasthenia gravis will develop at a later date; after surgical removal or radiation the chances are presumably greatly lessened.

A total of 13 patients with thymomas were treated by Williams,[37] 4 by irradiation alone. The other 9 were treated by thymectomy in addition to radiation. Of the 4 patients given irradiation only 1 responded well. In 3 treatment had to be interrupted because of tachycardia, a raised temperature and retrosternal pain, symptoms that Williams assumed to be due to a radiation mediastinitis. Nine patients were treated by irradiation before thymectomy; 1 died of metastases. Four responded well to radiotherapy. They were operated on three to six months after x-ray treatment. The dosage started at 50 or 100 r to the tumor daily. The limit was 4000 r in four weeks' tumor dose. Improvement when noted was in radiologic evidence of shrinkage of the tumor and improvement in the myasthenia. The sound procedure of radiotherapy for thymomas before operation thus introduced by Williams should be given a most extensive trial in other clinics.

Grob[28] found no striking improvement in his series of 40 irradiated patients, not all with tumors. Few achieved complete remission. His doses, however, were only about 2000 r. Similar results, with approximately the same amount of irradiation, were reported by me some years ago.

Irradiation of thymomas has been shown by Williams and others to be of value as a preoperative procedure, shrinking the tumor and, some surgeons think, making it more easily removable. Used as a form of treatment, moreover, in some cases, even when malignant tumors have been disclosed at operation, a prolonged remission in the myasthenia has resulted. The steps to be used in x-ray diagnosis are now well standardized. The use of radiation for treatment is still in the exploratory stage.

Experimental Aspects

Assay of Thymus Extracts

Forty-two glands removed from patients with myasthenia gravis by Keynes were assayed by Wilson,[38] using the isolated rat phrenic-nerve-diaphragm technic. The effects produced on the same preparation by *d*-tubocurarine were used as a standard for comparison. Control observations on thymus glands of normal adults, removed post mortem and tested in the same way, showed little or no neuromuscular blocking activity. The glands were assayed in groups, corresponding to the clinical effects produced by removal, the key to these groups being purposely withheld by the clinician from the investigator. Glands from clinical Groups A and B, in which the patients had complete or nearly complete remissions, demonstrated an increased neuromuscular blocking activity when compared with assays made from tissue removed from clinical Groups C and D.

Wilson and his associates[39] gave more details of the method used in a second paper, with the results and a discussion of the theoretical implications of his close correlation between the experimental and the clinical data. A suitable solvent for the gland was found in acetone, and a biologic test sufficiently sensitive for comparison of the activity of the extracts with that of *d*-tubocurarine on the phrenic-nerve-diaphragm preparation of the rat was described. The thymic extract depressed the response of the muscle twitch to indirect stimulation similar to that seen when curare was used. The results were quantitated. Extracts from a few but not all adult glands in nonmyasthenic persons produced an increase rather than a decrease in muscular contractions. Extracts of glands from children, however, reacted more like those from patients with myasthenia, showing high activity.

The series is too small to be considered conclusive. It appears that the thymus gland stores an active neuromuscular blocking substance. The amount extracted from a gland may not, however, bear any direct relation to the severity of the myasthenia, nor may the amount stored be of the same order as the amount released daily. The thymus gland may even not be wholly responsible for the production of this substance. Whatever conclusions are ultimately drawn, Wilson's study to date appears to be of distinct significance. It marks a step in advance since the work of Constant in 1949.

Blood Serum Studies

Other investigators continued the work on myasthenic blood in the hope that a curare-like factor could be demonstrated. Bergh,[40] using a nerve-diaphragm preparation from the guinea pig, rat and cat, had only negative or uncertain results but, as he suggests, the method employed for the biologic assays may have been insufficiently sensitive. With blocking agents, such as *d*-tubocurarine, decamethonium and succinylcholine, Bergh[41] also found differences in response in the phrenic-nerve-diaphragm preparations of 6 species of animals (guinea pig, dog, cat, rabbit, golden hamster and rat), thus suggesting variations in the motor end-plates of the experimental agents used.

Kures and Malek,[42] however, reported an active factor in the blood of myasthenic patients with the use of a neuromuscular preparation from the frog. The blood from 4 patients was tested; the changes recorded were not found in normal serum.

Schwarz,[43] using serum from temporarily untreated patients with myasthenia gravis injected intramuscularly into the forearm of a normal subject, produced marked weakness in the forearm and hand; this was overcome by neostigmine injected into the same muscles. No weakness was caused by similar injections of normal serum. In addition transfusion of a normal subject with blood from patients with myasthenia gravis did not produce any apparent changes in muscular strength, and a myasthenic patient receiving 4000 cc. of fresh blood was not benefited. Other investigators consider intramuscular injections an unsatisfactory method of experimentation.

Stuppler[44] studied 22 patients and came to the conclusion that a curare-like substance blocking the neuromuscular transmission was the most tenable theory to explain weakness in the disease. In denervated dogs he was able to obtain weakened myasthenic effects and demonstrate that neostigmine was effective even in the denervated muscle. He concluded that the therapeutic effects of neostigmine were twofold: an inhibiting action on the cholinesterase metabolism and stimulation of the muscle itself.

Schwarz, Price and Odell[45] noted in a few of their patients with myasthenia gravis a persistent elevation of the fasting serum phosphate level. The elevation was not associated with any changes in phosphatase activity, disturbance in calcium metabolism or skeletal abnormalities; renal-function tests were normal. In 1 patient the range was 5.0 to 5.2 mg. per 100 cc., and the level rose to 16 mg. four hours before death. A large thymus mass was found at autopsy. In an-

other patient the phosphorus determinations were 4.0 mg. per 100 cc. four months after thymectomy. Preoperative levels were 5.2 to 5.6 mg. per 100 cc. When a lyophilized thymic extract from young calves was injected subcutaneously a rise in both calcium and phosphorus levels was found in patients, control subjects and laboratory animals. The mechanism of this phenomenon was not clear.

Histochemistry of the Myoneural Junction

An excellent survey of the subject was provided by Denz,[46] taking into consideration the methods of Gomori (1948), Nachlas and Seligman (1949) and Koelle (1950). The histochemical staining of the junction of the rat diaphragm, when acetylthiocholine was used as a substrate, is due to the activity of specific cholinesterase. This esterase is the main enzyme in the synaptic gutter at the myoneural junction, with a small amount of nonspecific cholinesterase. An aliesterase is spread diffusely throughout the muscle fibers, without local concentration at the myoneural junction.

Ravin, Zacks and Seligman[47] believed that the method of Koelle leads to an erroneous localization of enzymatic activity. They presented a new method, providing for the specificity of the reaction for acetylcholinesterase in nervous tissue only. With fresh frozen sections enzymatic activity was demonstrated in the cytoplasm and cell membranes of neurocytes, in the neuropil and in myoneural junctions. Cell nuclei were free of enzymatic activity.

Demyelination from Organophosphorous Compounds

Barnes and Denz,[48] using three organophosphorous compounds (Mipafox, D.F.P. and T.O.C.P.) produced demyelinating lesions in chickens, rats and rabbits. Each of the drugs possessed marked anticholinesterase property, but it was believed that the acute toxic effects in animals could not be solely or directly related to their ability to inhibit cholinesterase. The demyelination was found in peripheral nerves and in the spinal cord. From these experiments it may be concluded that certain organophosphorus compounds cause structural changes in the nervous systems of animals. They may do so in man and, therefore, should be used cautiously.

Neuromuscular Transmission

Feldberg[49] continued his elucidation of the problem of synaptic transmission and neuromuscular block, upholding the acetylcholine theory in neuromuscular transmission on the basis of depolarization of the motor end-plate. He believed that depolarization can be demonstrated from the end-plate region of a muscle, or more easily from an end-plate without muscle, as in the electric organ of the torpedo fish. Acetylcholine apparently acts only on the end-plate, not on the neuromuscular transmission mechanism in the muscle itself. When the acetylcholine persists long enough at the end-plate the very strong depolarization current spreads to the adjacent parts of the muscular fiber, which in turn become depolarized and inexcitable, giving rise to block. Decamethonium, with its acetylcholine-like action, is also an effective neuromuscular blocking agent.

(To be concluded)

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MEDICAL INTELLIGENCE

STOKES–ADAMS ATTACKS AND CUSHING'S SYNDROME*

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CORONARY arteriosclerosis appears to be a common complication of Cushing's syndrome.[1] A case has been observed recently with Cushing's syndrome and Stokes–Adams attacks that were probably caused by coronary arteriosclerosis. A survey of the literature suggests that this is an unusual combination although the two conditions are probably related.

CASE REPORT

A 36-year-old housewife was referred to the Emergency Unit of the University Hospital with repeated fainting spells for the preceding 16 hours. The attacks, which occurred without warning, were accompanied by cyanosis and were followed by palpitation and dyspnea for a few minutes. There were no convulsions, and each episode lasted for only a few seconds. In 1949, at the age of 33 years, she had her first fainting episode. In 1950 and 1951 she had similar attacks, for which she did not seek medical advice.

At the age of 11 the menarche occurred, with irregularly spaced menstrual flow at intervals of 3 to 6 weeks. The periods finally stopped at the age of 28. Ovariectomy was performed on the left for a cyst at the age of 31, the right ovary being left intact. She had never been pregnant.

She had always had a moderate amount of hair on the extremities. At the age of 17 she noted the onset of baldness and the appearance of hair over the sternum, breasts and face and a definite increase over the legs and arms. Her beard required frequent shaving. She had always been moderately obese, but after the age of 23 she started to increase rapidly in weight while receiving desiccated thyroid. Her face had become rounded, and her obesity was limited to the trunk. In 1951 a physician made the diagnosis of Cushing's syndrome. Her general appearance was then the same, except for less marked baldness. The blood pressure was 158 systolic. An electrocardiogram revealed a 2:1 atrioventricular block, and the urine contained sugar. The 24-hour excretion of urinary 17 ketosteroids was 10 mg. X-ray therapy, consisting of 1200 r, measured in air, was applied to the pituitary fossa.

The patient was 157.5 cm. tall and weighed 84 kg. Her appearance suggested Cushing's syndrome, with a round face, moderate baldness, sparsity of hair over the occiput, truncal obesity, thin arms and legs and marked hirsutism, hair being present over the face, sternum and breasts, with a male distribution of pubic hair. No bison hump or pinkish abdominal striae were observed. Breast development was normal. Moderate arteriovenous nicking was seen in the optic fundi. The lungs were clear. The heart was not enlarged to percussion, and there were no murmurs. The rate varied between 30 and 40 beats per minute, and the blood pressure between 122/70 and 160/100 during the hospital course. Pelvic examination revealed an atrophic and inflamed vulva; the remainder of the general physical examination was not remarkable.

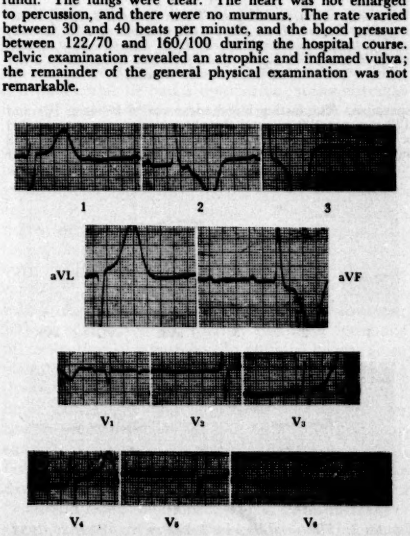

FIGURE 1. *Electrocardiogram Taken on November 25, 1952, Showing Complete Heart Block, with an Idioventricular Rhythm.*

Examination of the blood showed a red-cell count of 5,500,000, with a hemoglobin of 19.3 gm. per 100 cc., and a hematocrit of 60 per cent. The white-cell count was 7050, with a relative lymphocytosis (54 per cent). The erythro-

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cyte sedimentation rate was 1 mm. per hour. The urine had a specific gravity of 1.017, with a pH of 5, a + test for sugar and albumin. The sediment was normal, and the Sulkowitch test gave a greater turbidity than a control

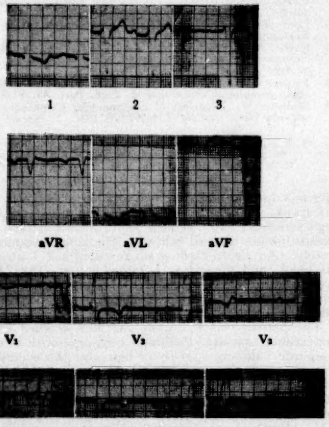

FIGURE 2. *Electrocardiogram Taken on April 6, 1953, Showing First-Degree Heart Block (PR Interval of 0.26 Second) and Left-Bundle-Branch Block (QRS Complex of 0.15 Second) in the Limb Leads (the Precordial Leads Show a 2:1 Atrioventricular Block).*

specimen. The fasting blood sugar varied between 101 and 172 mg. per 100 cc., and the glucose tolerance test revealed a diabetic type of curve. The serum cholesterol was 193 mg., the calcium 10.9 mg., and the phosphorus 3.9 mg. per

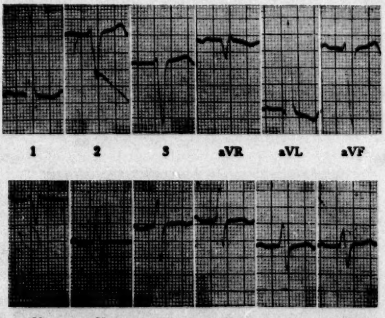

FIGURE 3. *Electrocardiogram Taken on November 30, 1953, Showing First-Degree Heart Block (PR Interval of 0.24 Second) and Left-Bundle-Branch Block (QRS Complex of 0.15 Second).*

100 cc.; the serum sodium was 147 to 151 milliequiv., and the potassium 4.7 to 6.0 milliequiv. per liter. Eosinophil counts varied between 90 and 100 cells per cubic millimeter. The arterial pH was in the range of 7.41 to 7.43. The 24-hour excretion of urinary 17-ketosteroids was 9.2 mg.; the corticosteroid was 2 mg. (normal 0.8 to 1.2 mg.), and the urine creatinine 0.14 gm. The uptake of radioactive iodine after a tracer dose was 22 per cent. On x-ray examination the pineal body was calcified, and the skull was within normal limits, with no frontal hyperostosis noted. An intravenous pyelogram revealed prompt excretion of the dye, with normal outlines of both renal shadows. No definite osteoporosis was evident in the spinal column. Fluoroscopic study disclosed minimal enlargement of the left ventricle.

About 1 hour after admission the patient lost consciousness, became extremely cyanotic and incontinent of urine and feces and had several grand-mal seizures. Even her respiration was thought to have ceased, and no heartbeats could be heard. An electrocardiographic tracing obtained shortly afterward showed complete heart block, with a ventricular rate of 38 beats per minute (Fig. 1).

She was given oxygen and intramuscular injection of ephedrine. During the next 24 hours she had several Stokes–Adams attacks. Therapy consisted of oxygen inhalation when needed and ephedrine, 25 mg. every 2 hours. The electrocardiogram changed from a complete heart block to 2:1 atrioventricular block, left-bundle-branch block and 1st-degree heart block (Fig. 2). She was discharged symptom free on ephedrine, 125 mg. a day. On this dosage no attacks occurred for 14 months after discharge (Fig. 3).

DISCUSSION

This patient presented the clinical picture of Cushing's syndrome in addition to compatible laboratory findings of erythrocytosis, relatively low eosinophil count, high fasting blood sugar and increased excretion of creatinine and 11-oxysteroid. In addition she had typical Stokes–Adams attacks, which have been defined by Parkinson et al.[2] as "episodes of loss of consciousness due to ventricular standstill, tachycardia or fibrillation or to their combination in a patient with heart block."

Many causes of complete heart block have been described, including congenital heart lesions,[1] vascular abnormalities affecting the atrioventricular node,[3] aneurysm of the aortic sinus[4] and even calcareous masses at the base of the aortic leaflet of the mitral valve, occurring after the age of fifty without relation to arteriosclerosis.[5] Rheumatic fever[6] and diphtheria are well known causes of complete heart block in children, the cardiac lesion after diphtheria usually being transient.[7,8] The majority of patients with Stokes–Adams syndrome have arteriosclerotic heart disease and coronary insufficiency, the incidence amounting to 75 per cent in some series.[1] Statistically, the commonest causes of the attacks in the younger age group have been previous infectious processes or certain congenital abnormalities in the absence of arteriosclerosis.

Through the wide use of ACTH, both experimentally and therapeutically, the cardiovascular abnormalities of Cushing's syndrome have been more fully understood. Deposition of lipid material in both the media and intima of the aorta and vessels has been noted in young people after the administration of cortisone or ACTH.[9] Arteriosclerotic changes of varying intensity have been described in 50 of 56 cases of Cushing's syndrome examined at autopsy.[10] A similar incidence of arteriosclerosis in this disease is reported by other authors.[11] More pertinent to the point under discussion are 2 specific cases, 1 in a

twenty-six-year-old woman with advanced coronary sclerosis and nephrosclerosis, and the other a twenty-eight-year-old woman who had a myocardial infarction in addition to severe generalized arteriosclerosis.[10]

In spite of the presence of arteriosclerosis in Cushing's syndrome hypercholesterolemia has not been a striking feature of the disease. Serum cholesterol values above 250 mg. per 100 cc. have been reported in 39 per cent of 56 cases.[10] Experimental evidence is also confusing. Extract of the adrenal cortex causes a definite increase in the serum cholesterol level in rabbits.[12] An average increase of 15 per cent has been seen in patients under cortisone therapy,[13,14] whereas other authors report a fall in the cholesterol level during short-term ACTH therapy.[15] Of perhaps greater significance is the fact that no change in the lipoproteins has been observed in human subjects.[16] It is apparent, then, that the precise relation of arteriosclerosis and Cushing's syndrome remains to be clarified. Definite atherogenicity of cortisone has been observed both in young human patients[9] and in chicks.[17]

Considering the high incidence of arteriosclerosis in Cushing's syndrome it is logical to attribute the Stokes–Adams episodes in the case reported above to this entity.

Summary and Conclusions

A case of Cushing's syndrome associated with Stokes–Adams episodes and complete heart block is presented. Clinical and pathological evidence in the literature suggests a causal relation in view of the observed high incidence of arteriosclerosis in women with Cushing's syndrome. The exact mechanism of this relation is not yet clear.

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CASE RECORDS
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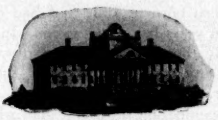

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 40281

Presentation of Case

A twenty-five-year-old Italian-born construction worker was admitted to the hospital because of persistent diarrhea.

The history was obtained chiefly from his wife because of a language barrier. As far as was known he had been in good health until eight months previously, when diarrhea developed, consisting of 3 to 5 watery, brown stools daily, without known blood, mucus or pus and without any noticeable pain or cramps. Several weeks later he had a nonspecific "uncomfortable feeling" in the abdomen that did not radiate and was not related to meals. At times he had distressing abdominal bloating after meals, sometimes relieved by passing of flatus. He believed that he had a low-grade fever at that time. About this time he visited an outside clinic, where examination of stools, x-ray studies and sigmoidoscopic examination were said to be negative. He was given liver injections as well as other medicine of an unknown nature, but diarrhea continued. About five months before entry treatment with cortisone was begun, at first 200 mg. and later 100 mg. daily, and this therapy had been continued up to the time of admission. In addition he was given vitamins and other medicines, without effect on the diarrhea. At that time he had as many as 8 or 9 bowel movements daily, but about two months later bowel movements changed to 2 brown, formed stools each day, and he regained his normal weight. This lasted only three weeks, however, after which the diarrhea returned. One month before admission a "cold and fever" developed, with such an increase in the diarrhea that he was awakened several times each night. The stools were frequently foul, but their character had apparently remained about the same. About three weeks before admission he began to have dull, aching pains in the knees, elbow and wrists but without swelling or redness of the joints. He had a mild fever (the temperature was never over 101°F.) on

occasion throughout his illness. He had also had dull pain from time to time below the umbilicus, occurring at any time of day and usually relieved by defecation. His weight had dropped from 157 to 126 pounds.

He had been born in Italy and had come to this country seven years before admission. In the past he had had only the usual childhood diseases; he did not know of any exposure to malaria, tuberculosis or typhoid fever.

Physical examination showed a man who appeared chronically ill but was not in acute distress. The head and neck were normal, and there was no lymphadenopathy. The heart and lungs were normal. The abdomen was tympanitic; there was no tenderness, masses or palpably enlarged organs.

The temperature was 102°F., the pulse 95, and the respirations 18. The blood pressure was 115 systolic, 55 diastolic.

The urine had a specific gravity of 1.015, and examination was otherwise negative except that the sediment contained 12 white cells and 15 red cells per high-power field. Examination of the blood revealed a hemoglobin of 16.7 gm. per 100 cc. and a white-cell count of 13,000, with 76 per cent neutrophils. The fasting blood sugar was 80 mg., the nonprotein nitrogen 14 mg., the total protein 5.6 gm., the albumin 4.0 gm., the globulin 1.6 gm., the calcium 8.0 mg., and the phosphorus 3.9 mg. per 100 cc.; the sodium was 133 milliequiv., the chloride 93 milliequiv., the potassium 3.0 milliequiv. and the carbon dioxide 31 milliequiv. per liter. The prothrombin time was 19 seconds (normal, 13 seconds). The oral glucose tolerance test gave a flat curve over a four-hour period. Heterophil-antibody and Widal and brucella agglutinations were negative. Stool specimens were "pale to light yellow" and negative for blood, ameba and enteric pathogens. A gastric analysis demonstrated no free acid before or after histamine.

A roentgenogram of the chest was normal. In a gastrointestinal series the esophagus was normal, and no organic lesions were seen in the stomach. The duodenal bulb appeared normal, but beyond this point, extending to the ileocecal valve, the small bowel showed grossly disordered motor function (Fig. 1). This appeared worse in the distal portion of the bowel. The mucosa was edematous, and many loops were slightly dilated; there was some puddling. Peristalsis, however, appeared normal, and the bowel was freely movable. Barium reached the cecum in two and a half hours. In an intravenous pyelogram the right-psoas-muscle shadow was not as clear as the left. The kidneys and ureters were normal; the bladder was never well distended with urine, and its dome disclosed irregular areas of pressure, which were probably due to diseased ileum adjacent to it. A barium-enema examination was negative. Gastroscopic study was incomplete owing to retained secretion but appeared to be negative. Cytologic examinations were negative, and a gastroscopic biopsy was reported as indicating "chronic gastritis." Sigmoidoscopic examination revealed reddened mucosa consistent with chronic diarrhea.

In the hospital the patient showed little change clinically and was weak and febrile. The temperature curve was persistently irregular ranging from 99 to 101 or 102°F. daily. The white-cell count ranged from 11,900 to 13,500. Four additional urinalyses demonstrated 3 to 10 white cells and 3 to 15 red cells and occasional hyaline and granular casts per high-power field. Despite supportive therapy he lost 6 pounds. On the eighteenth hospital day an operation was performed.

Differential Diagnosis

Dr. Alfred Kranes*: This history is simply that of a young man with diarrhea for eight months, weight loss, some fever and, more recently, joint pains without any joint swelling. The reliability of the history is open to question since it had to be taken through an interpreter, but we have to use what is presented to us. I am puzzled by the continued administration of cortisone for five months because it did not appear to have improved the patient in any way—it seemed to make no difference in the degree of diarrhea whereas joint pains appeared and the fever continued.

There is nothing helpful about the physical examination; it showed only a chronically ill person. The light-colored stools suggested the possibility of steatorrhea. They were described as foul, but nothing was said about foaminess or greasiness. It would be helpful to know whether he had steatorrhea and if there were excessive undigested muscle fibers in the stool.

Dr. Yang Wang: He did not have steatorrhea.

Dr. Kranes: I am reduced to depending very heavily on the x-ray findings, which I hope will turn out to be more helpful than they seem from the protocol.

Dr. John F. Gibbons: This one film from the barium-enema examination I put up to show that the cecum appeared normal and the appendix filled. Films were made three quarters of an hour, an hour and a quarter and an hour and three quarters after a barium meal. From the duodenal bulb down to the cecum the pattern of the mucosa is abnormal. The folds appear to be thickened, and there are areas of narrowing or spasm in the small-bowel loops. There is a tendency to segmentation or puddling of the barium that is not normally seen. The usual continuity of the barium stream and the feathery pattern that we normally see in the small bowel are lost. No areas are more involved than any others, and there are no regions where there is persistent narrowing. The small-bowel loops in the pelvis are separated from each other and do not fall together as they normally do. This pattern has been called a "disordered motor function" or "a deficiency pattern"

*Physician, Massachusetts General Hospital.

and there is nothing specific about it. It could be produced by a host of conditions—inflammations, allergies, nutritional deficiencies or neoplastic diseases within the abdomen (Fig. 1).

DR. KRANES: There is nothing characteristic about that. Could you say that the small bowel was itself structurally diseased?

DR. GIBBONS: I cannot say that. I can suspect that the mucosa is thickened.

DR. KRANES: Could this be the picture of sprue?

DR. GIBBONS: It could be except for the rapid transit time; within three quarters of an hour the barium had reached the cecum. In sprue liquid usually traverses the small bowel slowly, but the pattern itself could well be the picture of sprue.

FIGURE 1. *Anteroposterior View of the Stomach and Small Bowel, Showing Generalized Alteration of Mucosal Pattern in the Small Intestine.*

DR. KRANES: Could you exclude the possibility of widespread regional ileitis? I hesitate to use the term regional ileitis, because if this was ileitis, it was not regional.

DR. GIBBONS: I believe we can exclude that; it would be extremely unusual for the entire small bowel to be involved uniformly without "skip areas," or areas of relative fibrosis or narrowing.

DR. KRANES: Is the defect of the bladder outline present in the intravenous pyelogram?

DR. GIBBONS: The radiologist was referring to the concave effect of small-bowel loops in the pelvis. This does not suggest that the urinary bladder is diseased.

DR. KRANES: At least I can narrow the speculation about the area of the disease to the small bowel or its appendages and forget about other areas.

Until I was certain about whether or not steatorrhea was present, I had considered the possibility of sprue, but even without that knowledge it seemed like an improbable diagnosis since sprue is generally not febrile. Furthermore, this case lacks some of the other features of the disease. One would have expected glossitis by now and even anemia. A feature that suggests sprue is the flat glucose tolerance curve, but that is not specific. Any disturbance in which food is hurried through the small bowel would similarly lead to a flat glucose tolerance curve. Achlorhydria is too common to be helpful. Similar objections pertain to pancreatic insufficiency, in which the glucose tolerance curve may be diabetic.

Another possibility suggested by the history is a "generalized jejunoileitis" of a nonspecific type. To establish that diagnosis one would have to rely heavily on the x-ray films; yet the findings, Dr. Gibbons informs us, are certainly not those of ileitis. The entire small bowel was involved, which would be quite unusual. As he pointed out, there are usually normal areas between the diseased areas. One would also expect narrowed areas with such extensive ileitis.

DR. GIBBONS: I agree.

DR. KRANES: So that I shall have to explore further. Once one leaves this reasonably familiar ground, one enters the dangerous territory of the uncommon diseases diagnostically speaking; yet, it seems to me, this ground has to be explored. The first of these conditions that occurs to me is Whipple's disease or lipodystrophy intestinalis. Not many cases have been described,—perhaps about 50,—but many features of the illness fit in with that diagnosis. In the first place the patient under discussion was a man; the majority of the patients reported in the literature were men although usually of forty to sixty years of age rather than younger. Furthermore this patient had arthritis (I suppose I shall have to say arthralgia), and joint pains are an extremely common accompaniment of Whipple's disease. The arthritis, however, usually precedes the development of the gastrointestinal symptoms—often by weeks but more frequently by months or even by years in some cases; so that if this was Whipple's disease, it is disturbing that the arthritis developed after the intestinal symptoms were well established. The emaciation is common with any chronic diarrheal disease. Usually, Whipple's disease is not febrile, although some cases have been described in which moderate degrees of fever have occurred. This disease has interested me for a long time, primarily because of its possible relation to the various collagen diseases. It has much in common with them except for the obvious and striking histologic findings in the gastrointestinal tract and the mesenteric lymph nodes. I have already mentioned the fact that arthritis is a common accompaniment. Pleuritis, pericarditis and peritonitis are frequently found. In a certain number

of cases there has been a verrucous endocarditis almost exclusively confined to one leaf of the aortic valve. Whipple's disease, then, is much more than a disease of the gastrointestinal tract. Some cases have also been described with gross hematuria, and it is interesting that this patient had microscopical hematuria.

Before going any farther afield I might speculate about the operation. I should guess from the information supplied that it was probably an exploratory operation of some kind, performed to establish a diagnosis. I had supposed it was a laparotomy until I noticed Dr. Edward B. Benedict in the front row. It then occurred to me that I had to consider the possibility of a peritoneoscopy.

DR. DANIEL S. ELLIS: Dr. Benedict performed the gastroscopic examination.

DR. KRANES: Thank you.

If I had had to handle this patient and had had to choose between peritoneoscopy and exploratory laparotomy, I should have chosen the latter because it is very likely that a biopsy would be necessary. Dr. Benedict will tell me he can biopsy through the peritoneoscope, but it might have been advisable to remove more than could have been taken in that way. What was found and what was done constitute the crux of the situation. The surgeon may even have found that the bowel was grossly normal to inspection. Dr. Gibbons, is it not conceivable that the bowel looked grossly normal?

DR. GIBBONS: It is conceivable. Actually, we are seeing a cast of the small-bowel lumen.

DR. KRANES: It is difficult to see what, if any, remedial surgery could have been done under the circumstances. If the disturbance was confined to the entire small bowel it is difficult to believe that the surgeon could have removed anything from the bowel that might have helped this patient. Could he have removed something for diagnostic purposes? That is also difficult to believe because when the whole bowel is diseased it is risky surgically to remove a small segment of it.

The surgeon may have encountered a large mass of mesenteric lymph nodes. If that was so, what did these lymph nodes contain? I have already discussed Whipple's disease, in which the mesenteric lymph nodes are diffusely involved with infiltration of fat lipophages and giant cells. There are two other possibilities, one of which is extensive mesenteric tuberculosis—tabes mesenterica, it used to be called. One sees this infrequently these days. If the mesenteric lymph nodes had been so extensively involved as to interfere with lymphatic drainage of the small bowel, this distorted appearance of the bowel with mucosal edema would have been noted. If this had been malignant lymphoma, the third possibility, the x-ray appearance might have been expected, but it is unusual for the mesenteric lymph nodes to be the only site of lymphoma. One would like to find evidence of it elsewhere, as in the superficial lymph nodes, the spleen or the mediastinum. Of the two possibilities I should favor tuberculosis.

I have not made a diagnosis; I do not think I can, but the hematuria deserves further comment. I assume that the renal function was normal since I have no reason to assume that there was renal insufficiency. I do not know that it is worth while exploring the question of hematuria further because my guess is that the patient was operated on, something was removed and he survived the operation. Consequently, it is likely that Dr. Morgan will not be able to tell us the reason for the hematuria. I might speculate a bit, however; after seeing the x-ray films I wondered whether it might have been due to irritation of the bladder by overlying diseased bowel. We now know that renal lesions occur with chronic intestinal diseases; one such case was discussed here by Dr. Trevor Cooke,* of England. These renal lesions are primarily tubular lesions and ordinarily are not expected to produce hematuria. In the cases in which these lesions are found, renal insufficiency is not present, and hematuria is unusual. Of the diseases that I have mentioned the only one that will also explain the hematuria—and in a young person one would like to explain all the findings on one basis if possible—is tuberculosis. If this patient had abdominal glandular tuberculosis, he may also have had a concomitant renal tuberculosis.

Finally, in a patient who had hematuria, fever and joint pains, one has to mention the possibility of polyarteritis, which always seems to be dragged in by the tail to explain any obscure illness. Chronic diarrhea is not a symptom of polyarteritis, although I suppose if I had time to review the literature on the subject I could find 3 or 4 cases that showed it. I do not know why it should not be since the vessels involved may be not only in the mesentery but also in the wall of the bowel. One wonders why diarrhea is not a more common symptom.

I cannot actually make a diagnosis; all I can do is to suggest the possibilities. I shall have to name three or four.

DR. EDWARD F. BLAND: Choose one; that is what we had to do on the ward.

DR. KRANES: If I have to name one—I had hoped you would not pin me down—I shall have to put it in the connective-tissue group of diseases, either Whipple's disease or polyarteritis. Beyond that I should have to say regional enteritis or mesenteric tuberculosis, but I am not happy about either of those conditions.

DR. BLAND: Personally, I favored lymphoma. Dr. Wang was on the service at the time. Perhaps he will tell us what he thought.

DR. WANG: During the first few days, the service actually did favor intestinal and renal tuberculosis to

*Case Records of the Massachusetts General Hospital (Case 40081). *New Eng. J. Med.* 250:334-340, 1954.

explain the diarrhea and hematuria and sent the urine for guinea-pig inoculation. Somewhere along the line the weight of popular opinion swung in favor of lymphoma, and we were carried along by the tide. Since therapy in this case was to be either the antituberculosis drugs or cortisone, we thought it necessary to operate to establish an exact diagnosis.

DR. ELLIS: Two reasons why the diagnosis of lymphoma was favored over tuberculosis are that the temperature chart suggested a Pel–Ebstein type of fever and that the x-ray films showed the bowel to be fairly movable within the peritoneal cavity; there was no plastic process such as one expects with tuberculous peritonitis. It was obvious that one could not make a diagnosis without exploration, and that is what was done.

DR. FARAHE MALOOF: Is it not also true that peripheral lymph nodes are not seen with the abdominal lymphadenopathy of lymphoma?

DR. KRANES: That is usually true of the retroperitoneal type of lymphoma.

CLINICAL DIAGNOSIS

Malignant lymphoma of mesenteric lymph nodes.

DR. ALFRED KRANES'S DIAGNOSIS

?Whipple's disease or polyarteritis nodosa.
?Regional enteritis or mesenteric tuberculosis.

ANATOMICAL DIAGNOSIS

Tuberculosis of mesenteric lymph nodes.

PATHOLOGICAL DISCUSSION

DR. WINFIELD S. MORGAN: Are any of the surgeons here who were at the operation?

DR. SIGURD B. GUNDERSEN: At operation there was a small amount of free, clear fluid in the peritoneal cavity, and there were multiple small nodules over the entire small intestine from the ligament of Treitz to the ileocecal valve measuring from 1 mm. to 3 mm. in diameter. In the small-bowel mesentery there were lymph nodes measuring from 1 cm. to 3 cm. in diameter. We could see dilated lacteal glands over the surface of the small bowel. Several areas had developed into indurated masses, but I could not be sure that there was any ulceration within the small bowel or any ulcer within its lumen. We did not open it.

DR. MORGAN: The main specimen received in the laboratory was a mesenteric lymph node that showed microscopically a typical picture of caseous tuberculosis. In addition we received several small nodules from the serosal surface of the bowel; microscopically, these proved to be portions of dilated lymphatic channels showing focal nodular proliferation of reticuloendothelial cells within the lumen. There is little doubt that the pathogenesis of the changes in the bowel was the one Dr. Kranes proposed—namely, extensive mesenteric-lymph-node involvement with blockage to the lymphatic drainage, the back pressure resulting in dilatation of the more distal lymphatic channels and diffuse edema of the intestinal mucosa. Would that fit with your interpretation of the x-ray changes, Dr. Gibbons?

DR. GIBBONS: That appears to be the only reasonable explanation for the diffuse process in the bowel.

DR. KRANES: In former days, when this condition was seen more frequently than it is seen today, diarrhea was not too uncommon a symptom, nor was steatorrhea.

A PHYSICIAN: Was the spleen enlarged at operation?

DR. GUNDERSEN: No; it was not.

CASE 40282

PRESENTATION OF CASE

A fifty-five-year-old paper-box maker was admitted to the hospital because of dyspnea and cough.

For ten years the patient had experienced exertional dyspnea. In the year before entry he had frequent "colds," during which he had orthopnea relieved by one or two pillows and a cough productive of moderate amounts of foamy, white sputum. These attacks were not usually incapacitating. Five months before admission, during another "cold," swelling of the right ankle was noted, and he was treated with "heart pills" and "cough medicine." Three weeks before admission dyspnea and cough again became more noticeable, and in the past week orthopnea became so severe that he had to sleep sitting up. He had ankle edema, but continued to work. He also had numerous epistaxes after blowing his nose that lasted about five minutes. Two days before entry red, painless spots appeared on the legs. The next day he consulted his physician, who discovered bilateral moist basilar rales, hepatomegaly, "purpuric lesions on both lower legs," normal blood pressure and a regular pulse at a rate of 104. There was no history of chills, joint pains or urinary symptoms.

For the past twenty or twenty-five years the patient had worked in a paper-box factory, where the air was dusty; however, he knew of no exposure to silica, cotton, wool or asbestos dusts. Eighteen years before admission a splenectomy was performed after trauma to the left side.

Physical examination revealed a thin man who appeared to be chronically ill. The neck veins were distended with the patient sitting at 45°, and the deep jugular pulsations were visible. The left cervical and a few axillary and inguinal lymph nodes were soft, discrete and freely movable. Transient groans and wheezes were heard throughout the chest; there were moist inspiratory rales at both bases, more marked on the left. The apex of the heart was 2.5 cm. to

the left of the midclavicular line. The pulmonic second sound was greater than the aortic. There was a short, high-pitched Grade 2 apical systolic murmur together with an apical mid-diastolic rumble with a presystolic crescendo. A loud mitral first sound and a split "scratchy" second sound were heard along the left sternal border in the fourth intercostal space. A gallop was audible after slight exercise. The liver was slightly tender; its edge was palpable 4 finger-breadths below the right costal margin. There was slight bilateral costovertebral-angle tenderness. A purpuric rash was observed over both legs, but no peripheral edema was present.

The temperature was 101°F., the pulse 100 and regular, and the respirations 22 per minute. The blood pressure was 128 systolic, 80 diastolic.

Urinalysis was normal. Examination of the blood demonstrated a hemoglobin of 13.5 gm. per 100 cc. and a white-cell count of 15,600, with 39 per cent mature and 14 per cent immature neutrophils, 42 per cent lymphocytes and 5 per cent monocytes. The serum nonprotein nitrogen was 21 mg., and the total protein 7.9 mg. per 100 cc. The prothrombin time was 14 seconds (normal, 15 seconds). The cephalin flocculation was + + + in twenty-four and + + + + in forty-eight hours, and a bromsulfalein test showed 13 per cent retention of the dye in forty-five minutes. The sedimentation rate was 0.6 mm. per minute. The hematocrit was 45 per cent. Stool guaiac tests were negative. Cultures of the sputum grew out moderate *Neisseria catarrhalis*, abundant *Haemophilus influenzae*, abundant alpha-hemolytic streptococci and moderate Group A pneumococci. On throat culture a few Group A pneumococci and abundant diphtheroids were present. Three sputum specimens were found unsatisfactory for cytologic study; another specimen was negative for tubercle bacilli. Two of four blood-culture flasks grew out *Staphylococcus albus*. An electrocardiogram demonstrated a regular sinus rhythm at a rate of 100. The PR interval was 0.16 second, and the QRS interval 0.12 second; the R waves were slurred in Leads 1, aVL, V_5 and V_6, the S waves were deep in Leads V_1, V_2 and V_3, the ST segment was sloping in Leads 1, aVL, V_5 and V_6, and the T waves were inverted in Leads 1 and aVL, diphasic in Leads V_5 and V_6 and tall and peaked in Leads V_2 to V_4.

Roentgenographic study of the chest with fluoroscopic and barium-swallow examinations disclosed that the right upper lobe was slightly reduced in size and contained abnormal linear and mottled densities, probably old. There were also minimal changes in the left upper lobe. No definite cavities were recognized. The barium-swallow examination did not reveal displacement of the esophagus.

The patient was treated with digitoxin, penicillin, streptomycin, sulfadiazine and Hykinone, but continued to have elevations of temperature to 101.5°F. and of pulse to 110. Coughing also persisted. The white-cell count remained elevated, and on the seventh hospital day was 17,000. On the fifteenth hospital day, immediately after using a bedpan, he complained of a burning, nonradiating substernal pain and dyspnea. This was accompanied by much apprehension, but no nausea, vomiting or sweating. The pain lasted twenty minutes and left a residual ache in the left shoulder and arm. Physical examination and electrocardiograms showed no change from the findings on admission. The patient became comfortable after receiving sedations. Three hours later, however, he began to move about restlessly, became cyanotic and died.

Differential Diagnosis

Dr. John Homans, Jr.*: This is a story of a fifty-five-year-old man who, ten years before admission, had his first symptoms of cardiac failure. We later learn from the physical examination that he had signs of mitral stenosis, so we may assume that he was suffering from chronic rheumatic heart disease. Five months before admission, during a cold, swelling of the right ankle was noted; that is important. Ankle edema from cardiac causes should be bilateral or beginning on the left and becoming bilateral, because of the crossing of the artery and vein to the left leg. I therefore think that this may have been the beginning of a thrombophlebitis. Three weeks before admission signs of congestive heart failure again became evident, and it was noted that he had, I assume, bilateral ankle edema. He suffered from nosebleeds, and his doctor noted, besides the signs of congestive heart failure, purpuric lesions on both legs. Both these will be discussed more fully later. It is not stated in this history whether the patient had fever.

Physical examination on admission to the hospital showed signs of congestive heart failure, and there were murmurs and other signs of mitral stenosis. The liver was enlarged, and the purpuric rash was still seen over the legs, though the edema had gone. For the first time the temperature was reported to be elevated, with the same pulse rate as noted previously.

The important findings in the laboratory work are that there were no red cells in the urine, no anemia and an elevated white-cell count, without an increase in neutrophils. The bromsulfalein retention and cephalin flocculation tests indicated, I believe, no more than congestion in the liver. The sedimentation rate was only slightly elevated. Sputum and throat cultures showed no predominant organism, and a sputum specimen was negative for tubercle bacilli. Two blood cultures demonstrated *Staph. albus*. This organism, though ordinarily not a pathogen, may on occasion act like one and may be the cause of subacute bacterial endocarditis. I do not believe that the electrocardiogram is particularly helpful. It could mean that he had a certain amount of coronary-artery disease. May we have a review of the x-ray films of the chest, Dr. Gibbons?

*Assistant in medicine, Massachusetts General Hospital.

DR. JOHN F. GIBBONS: The first films of the chest and another set of films made three days later show moderate prominence of the pulmonary artery of the cardiac silhouette but no gross cardiac enlargement. The lungs are emphysematous; both leaves of the diaphragm are low, and the anteroposterior diameter of the chest is increased. The size of the right upper lobe is diminished, and extensive linear densities extend from the lung roots to the periphery in this lobe. There are several smaller scars in the left upper lobe. In the left costophrenic sulcus there is an irregular shadow of increased density, which, over a period of three days, increased in density but not in size.

The densities in the upper lobes could well be the result of old, inactive tuberculosis. The shadow in the left costophrenic angle seems to represent a more acute process since it had diminished in size and almost completely disappeared on a film made twelve days after the original roentgenogram.

DR. HOMANS: Could the shadow in the left costophrenic angle represent a small pulmonary infarct?

DR. GIBBONS: Yes; that is possible, although not definite.

DR. HOMANS: In summary, this man with rheumatic heart disease, though he had his first symptoms of congestion ten years before admission, failed rapidly and died in three weeks. The ordinary reasons for such a course are the development of recurrent rheumatic fever, subacute bacterial endocarditis or some pulmonary or systemic infection. I am given no leads to infection outside the chest. The chest x-ray films apparently showed only old tuberculosis, and one sputum study was negative. As far as rheumatic fever is concerned, it may exist with no symptoms at all or with just a low-grade fever. Evidence of rheumatic activity is often found at autopsy when there was no clinical suspicion of it. Nosebleeds may be evidence of a rheumatic state. The patient ran an elevated pulse, but it was not stated what his temperature was; in the hospital, the temperature and pulse seemed about in proportion.

I favor bacterial endocarditis as the cause of this patient's terminal illness. There were two positive blood cultures out of four, and although it is possible that the organisms were contaminants, I shall accept them at their face value. He had a purpuric rash on the legs that was present with or without edema and may have represented the only evidence of embolic phenomena. The elevated white-cell count and sedimentation rate do not rule any infection in or out. The spleen does not enter into the discussion since it was absent, unfortunately. It was not stated in what dosage antibiotics were given, so the fact that they were used does not necessarily rule out bacterial endocarditis.

On the fifteenth hospital day immediately after using a bedpan (the classic circumstance for having a pulmonary embolism) the patient had a pain, which could have been due to embolism or coronary occlusion. Unfortunately, the pain of pulmonary embolism can mimic the pain of coronary occlusion, or the embolism may set off a coronary occlusion, so that without evidence of acute cor pulmonale on the electrocardiogram and on physical examination, or electrocardiographic evidence of an acute myocardial infarct, I see no way to distinguish these two. I now go back to the episode of swelling of the right calf, which, with the terminal episode, I think favors embolism. This brings up the possibility that the entire story was due to repeated attacks of pulmonary embolism. It is certainly possible though I do not see how the diagnosis could be made positively. There was no report of physical examination of the legs except the note that they showed no edema. There is only one possible, small infarct shown in the lungs. Of course, the fact that there were no more infarcts does not preclude the possibility of emboli, for the emboli themselves cast no shadows. The description of the fever does not state whether it was steady or whether there were periodic spikes of temperature, pulse and respirations. He died in three hours, which is consistent with either embolism or coronary thrombosis.

My impression is that this man had rheumatic disease with mitral stenosis. I think that bacterial endocarditis developed and that the terminal episode was a pulmonary embolism coming from a thrombophlebitis present in the legs.

DR. WINFIELD S. MORGAN: Dr. Rasmussen, would you tell us the opinion on the ward?

DR. HOWARD RASMUSSEN: The initial impression on the ward was that this man had rheumatic heart disease with mitral stenosis and congestive heart failure. In addition he was thought to have an acute pneumonitis and possibly subacute bacterial endocarditis. After a series of blood cultures antibiotics were started for the presumed pneumonia. He never received these drugs in adequate doses for treatment of an endocarditis. The fever did not disappear on this therapy, and this fact, together with the clubbing and unexplained purpura, worried us. The question of possible cirrhosis of the liver was raised by the hepatomegaly, the history of alcoholism and the abnormal values of the chemical tests of liver function. Our impression of the terminal episode was similar to that of Dr. Homans — that is, either pulmonary embolus or acute coronary occlusions.

CLINICAL DIAGNOSIS

Rheumatic heart disease, with mitral stenosis and congestive heart failure.
Acute pneumonia, ?subacute bacterial endocarditis.
?Cirrhosis.
Acute myocardial infarction or pulmonary embolus.

DR. JOHN HOMANS, JR.'S, DIAGNOSES

Rheumatic heart disease, with mitral stenosis.
Bacterial endocarditis.
Pulmonary emboli from thrombophlebitis.

Anatomical Diagnoses

Rheumatic heart disease, old, with chronic endocarditis of mitral and aortic valves (bicuspid).
Acute bacterial endocarditis, Staph. aureus, *mitral and aortic.*
Marked narrowing of coronary ostium.
Bronchiectasis, right upper.

Pathological Discussion

Dr. Morgan: At autopsy there was no evidence of any significant degree of congestive heart failure, and the pleural and peritoneal cavities were free of fluid. The liver was moderately heavy, weighing 1900 gm., and microscopical study showed moderate acute congestion. The kidneys were normal. The lungs were slightly edematous and congested and weighed 1000 gm. In the right upper lobe, corresponding to the area of increased density in the x-ray films, there was considerable bronchiectasis, with adjacent chronic pneumonitis and fibrosis. The reason for the bronchiectasis was not found, and it appeared to be of rather long duration. There were no pulmonary emboli.

The heart was within normal limits in size, weighing 330 gm. Although the mitral valve showed evidence of old rheumatic involvement, with thickening and shortening of the chordae tendineae and focal calcification, the orifice was not greatly narrowed, and it admitted 2 fingers freely. At one commissure, overlying a fibrous and partially calcified portion, there was an ulceration measuring 0.3 by 0.7 cm. coated with soft, reddish-gray, fibrinous material. The aortic valve also disclosed old rheumatic disease and contained rounded, calcareous deposits on the sinus side of the cusps. The anterior and posterior cusps were fused, forming a bicuspid valve, and there was an area of ulceration similar to but smaller than that found on the mitral valve. Microscopical sections through both valvular ulcerations revealed dense collagenous thickening of the leaflets and vascularization, reflecting the original rheumatic injury, with a superimposed endocarditis consistent with about a month's duration.

The endocarditis was characterized by a superficial layer of hyalinized fibrin, with organization and inflammatory infiltration of the deeper portions, the cellular infiltration being composed of neutrophils, mononuclear leukocytes and occasional eosinophils. Although there were relatively superficial foci of finely granular calcification that could have represented calcified bacteria it is unlikely that this change was effected by the antibiotic therapy in the short period that it was given. No recognizable bacterial colonies were observed in any of multiple sections. The ulcerative nature of the endocarditis, the apparent fact that the offending organism was a *Staph. aureus* and the short duration of the illness make it more likely that the complication that developed was an acute rather than a subacute bacterial endocarditis. No evidence of embolization was found in the other organs, and there was no glomerulitis of the type frequently seen in cases of subacute bacterial endocarditis.

Concerning the immediate cause of death in this man, the autopsy findings permit only speculation. The terminal episode was characterized by substernal pain and dyspnea lasting twenty minutes and leaving a residual ache in the left shoulder and arm. This certainly suggests a coronary origin, but examination of the heart failed to show myocardial infarction, either old or recent, and the coronary arteries were soft and widely patent throughout. There was one finding, however, that might explain the sudden death—the ostium of the left coronary artery was narrowed to about 1 mm. by the calcareous deposits on the aortic valve. It seems very possible that spasm or some other mechanism compromised this very small orifice further and produced, in effect, occlusion of the vessel, resulting in death.

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DIASTOLE

THE June issue of *Modern Medicine*, the journal that appears each month actually prior to its date of publication, contains a brief editorial "On Saving Time," by its dynamic and scholarly editor-in-chief, Walter C. Alvarez. Dr. Alvarez, who has the capacity for doing more interesting and useful things in a moment than many men do in a millennium, champions, in this instance, the policy of utter efficiency, whereby the talented and the highly trained, in their daily activities, perform only those deeds that require their specialized talents and training, and perform them unremittingly, leaving all ancillary tasks to less accomplished assistants.

Thus really important surgeons spend their operating hours marching and countermarching between two operating rooms where trained teams make incisions through which the craftsman executes his deeds of skill and daring, and on his clocked departure close them again. Electronic dictating machines are recommended for the really busy physician, and trained squads of secretaries who, like vestal virgins, tend incessantly the fierce fire that burns within the master mind. For not a moment of the leader's precious time must be wasted ere he falls victim to the inevitable coronary debacle or suffers too many and too large bites from the cerebral cortex.

The idea of an environmental subservience to the supercreature has its fascinating side, like the contemplation of those efficient machines with their supporting teams that print newspapers, weave textiles or paste the labels on tomato cans. But are there not two sides to every argument? Attractive as the concept of total efficiency may be, is it not somewhat impractical as well as a trifle merciless when applied to the human organism? Is it not perhaps essential for even the ablest executive to work in a sort of crude rhythm, with periods of magnificent accomplishment alternating with interludes, however brief, of performing from choice the simplest and most mechanical tasks?

It may actually increase his effective working time, over the years, if the eminent surgeon, physician or executive occasionally slips off his pedestal and reflects on the importance of being unimportant—an ancient aphorism but one that still occasionally applies. Wordsworth, in recommending the spatial limitations of the sonnet, notes that one of the most indefatigable of nature's workers observes the same rules of alternating activities:

> —bees that soar for bloom,
> High as the highest peak of Furness fells,
> Will murmur by the hour in foxglove bells.

Efficiency, the god of mechanical achievement, has its sinister aspect like other pagan idols. It is the god of the assembly line and the superhighway and the epinephric thrill of going places fast. It is responsible for an obsessive belief in the necessity of working intensively in order to save time that can be

spent in working still more intensively. It cuts the corners, it removes the trees that the road may be straightened, it abhors rumination, it is death on dalliance, diversification and digestion.

Even in the face of his requirement that "A very busy man should never be doing work which could be done for him by a girl," it may be supposed that the very human Dr. Alvarez, to whom general competence comes easily, might himself give support to a movement started in the interest of a salutary degree of inefficiency!

THIRD ANNUAL REPORT OF AMERICAN MEDICAL EDUCATION FOUNDATION

THE American Medical Education Foundation, established under the auspices of the American Medical Association to seek financial succor for the 79 medical schools of the country, has recently issued its third annual report. The reasons for establishing the Foundation are too well known to be given in detail here. The medical schools have long been faced with increasing operative costs on account of complicated teaching technics and advances in medical science, the necessity for increased salaries in order to obtain and hold good teachers, and the decline in purchasing power of a dollar that is also becoming relatively scarcer, so far as education is concerned, as income from traditional sources declines.

The important and encouraging fact brought out by the present report is that of continuing progress toward the goal of $2,000,000 a year in contributions derived from or through the medical profession. For the first time the sum collected has exceeded $1,000,000, the gross receipts in 1953 having been $1,089,963, representing an increase over 1952 of $183,409, or 32 per cent. Of even greater importance is an increase of 149 per cent in the number of individual contributors, from 7259 in 1952 to 18,176 in 1953.

A considerable part of this sum may be classified as automatic giving, since it consists of the $500,000 that the American Medical Association has so far donated each year to the fund. The figures show, nevertheless, a generally healthy gain, physicians having given independently $91,392 in 1951, $291,478 in 1952 and $467,217 in 1953. In the last two years this sum has increased substantially over the amounts given by medical societies and associations other than the American Medical Association, reversing the ratio of 1951, when such associations gave $116,380 compared with the $91,392 given directly by physicians. The contributions of associations and societies have maintained a substantial level, amounting to $113,232 in 1952 and $118,200 in 1953.

Total figures show that the physicians of the country, through the American Medical Education Foundation, are slightly in the lead over the National Fund for Medical Education, organized to seek contributions from business and industry. Of the nearly $5,000,000 so far made available by the two organizations the producers of medical care are responsible for more than its consumers.

V. A. SAVES MONEY

THE Veterans Administration, by operating mental-hygiene clinics at a cost 70 to 80 per cent lower than that of hospitalization in even the most economically operated hospitals, now saves more than $2,000,000 a year, according to a recent release from the Administration's Information Service.

More psychiatrists are needed to man the clinics, however, in order to help care for as great a proportion as possible of the half-million veterans with service-connected psychiatric and neurologic disabilities. Only service-connected cases are eligible for both outpatient clinic care and hospitalization; consequently it is in the most eligible group that this considerable saving is effected.

The medical profession will be unanimous in approving this policy of an economy-minded Veterans Administration, and it is hoped that the clinics will not long lack the necessary psychiatric personnel.

Adulteration of Castor Oil. — *It is hardly possible to conceive that any person can be base enough, for the sake of enriching himself, to be guilty of adulterating articles intended for food or medicine; . . . but we will simply allude to the fact of the extensive sophistication of castor oil, by the use of lard oil.*

Boston M. & S. J., *July 19, 1854*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BURKE — Francis R. Burke, M.D., of Quincy, died on June 22. He was in his seventy-eighth year.

Dr. Burke received his degree from Harvard Medical School in 1903. He was a member of the Massachusetts Board of Examining Physicians, Boston Orthopedic Club, American Association of Industrial Physicians and Surgeons, the staffs of the Quincy and Milton hospitals and New England Hospital for Women and Children and was a former member of the Orthopedic Clinic, Quincy Board of Health,

and a fellow of the American College of Surgeons and the American Medical Association.

He is survived by his widow, a daughter, a son, a sister and a grandson.

WOODBURY — Stillman P. Woodbury, M.D., of Millers Falls, died on June 12. He was in his ninety-seventh year.

Dr. Woodbury received his degree from Long Island College of Medicine in 1887. He was formerly school and town physician and was a member of the staffs of Franklin County Public and Farren Memorial hospitals.

He is survived by a daughter.

CORRESPONDENCE

ART OF LETTER WRITING

To the Editor: Why such exercise over the lack of medical correspondents? Has the editor tried being one? American medical literature is of poor quality. Why? The two agents in the case may be discussed, author and editor.

Editors, as a group, have demanded a style of scientific writing hardly conducive to informal statement. This style is absolutely *de rigueur:* formal, in the third person, "objective" and cut to the point of cryptic obliteration. The contents must have momentary popularity and fit the editor's most recently rearranged prejudices. Technical statement must be dead lest the personal slip in.

Now the correspondent. He must be pleasing and write in the editor's style. He must be aware of the times. Coming through the route of research, facts and discoveries do not make him particularly literate. The medical scientist shudders to think that one of his number would waste valuable time trying to find adequate means of expression with literary skill! Having selected the journal, he sets out with a bag of obscure references and complex and esoteric terms to dazzle the reader, calling it objective writing. Making it short but not directly dealing with reality, and cloaking it in words beyond comprehension, is called scientific. Insistence on formal statement has probably killed more would-be medical writers than anything else.

In contrast to their American counterparts both author and editor have a quite different approach in Great Britain, where editors seem to take a less rigid approach to the matter; livelier expression is encouraged, and the future outstanding contributor is led to his place by easy stages. Although much of the output is obviously not too important, high standards are maintained. In contrast, our writings are ponderous; we take ourselves altogether too seriously!

What should be done? This old problem is one that at present is being widely discussed. One doubts if much can be done as long as our training backgrounds, ideals and conceptual bases of work remain as they are today. After nearly two hundred and fifty years of medical writing, American physicians of literary stature number not more than six. O. W. Holmes, William Osler and Weir Mitchell come to mind.

Editorial encouragement brought forth this epistle. Obviously of no profound scientific value, it may at least purport, though written in current style, to be personal and, it is hoped, lively and of some present joy.

ANDERSON NETTLESHIP, M.D.

Little Rock, Arkansas

Note: The *Journal's* editorial of March 25, "To the Editor—" ended with the suggestion that some of the American journals "might be a little livelier were their readers to express themselves more freely through the informal vehicle of correspondence." — ED.

TREATMENT OF MIGRAINE

To the Editor: With great interest I have just read the paper by Graham on the rectal use of ergotamine tartrate and caffeine alkaloid for the relief of migraine in the June 3 issue of the *Journal.* In contrast to Dr. Graham's recommendation of suppositories containing a cocoa-butter base and with a dosage of 1 mg. of ergotamine tartrate and 100 mg. of caffeine alkaloid, we dispense suppositories pressed from a polyethyleneglycol base consisting of carbowax 1500, 1 gm., or 4000, 2 gm., with a finely crushed tablet of 1 mg. of ergotamine tartrate (these tablets being the sole supply of ergotamine tartrate in the Netherlands).

If the results with these carbowax suppositories (though far better than with suppositories containing a cocoa-butter base) are not favorable we advocate the addition of 50 mg. or 100 mg. of caffeine citrate to each suppository. By the addition of this much more soluble caffeine citrate the reliability of this method of treatment increased from about 60 per cent with cocoa-butter base and over 85 to 90 per cent with carbowax base to nearly 100 per cent.

Several patients also had to take up to 6 tablets of ergotamine tartrate by mouth to relieve an attack and (though at first they objected to the use of rectal suppositories) now find the method quite efficacious, usually even without the addition of some caffeine citrate to the suppositories.

Our impression, like Dr. Graham's, is that the rectal route for this medication is to be preferred to hypodermic injections, which many sufferers are often unable to obtain just at the onset of an attack.

Since it is sometimes contended that the content of ergotamine tartrate in these suppositories might decrease by storage only freshly pressed suppositories are delivered by the chemist, and not more than 6 at a time.

The polyethyleneglycol suppositories dissolve in the rectum. Because the melting point of the carbowax base is between 40 and 50°C., it is not necessary to keep them in a refrigerator. They are carried in the handbag as easily as tablets.

L. A. WESLY, M.D.
Medical Adviser
Rotterdam Sick Clubs

Rotterdam, Holland

EVALUATION OF POLIOMYELITIS-VACCINATION PROGRAM

To the Editor: The vaccination of children, which is the first step in the poliomyelitis-vaccine field trials sponsored by the National Foundation for Infantile Paralysis, has now been completed. The successful launching of the project is due substantially to the splendid voluntary co-operation of medical societies and practicing physicians in the trial areas.

More than 600,000 children have received 3 inoculations in the field test of the trial vaccine developed by Dr. Jonas E. Salk, of the University of Pittsburgh. The emphasis now shifts to the evaluation study under the direction of Dr. Thomas Francis, Jr., University of Michigan School of Public Health. The validity of evaluation is dependent on data gathered on poliomyelitis cases in the test groups, including children in the first three grades of school who did not get vaccine.

Data on cases among family members of participating children are an integral part of the study. Because the number of cases of poliomyelitis among test groups may not be large it is essential that all cases be completely reported. Early diagnosis, prompt reporting and follow-up study and the obtaining of necessary epidemiologic information and laboratory specimens are important factors in the evaluation.

An outline of procedures and copies of necessary forms have been sent to local and state health authorities. It is important that physicians in areas where vaccinations were not given co-operate in the study by notifying local or state health officers of cases occurring among children who participated in the trials and then moved to another area and those who go to summer camps. Local health officials also

need information on participating children who receive injections of gamma globulin.

This phase of the study is largely dependent on the wholehearted co-operation of practicing physicians.

HART E. VAN RIPER, M.D.
Medical Director
National Foundation for Infantile Paralysis
New York City

REVOCATION OF LICENSE

To the Editor: At the meeting of the Board of Registration in Medicine held May 20, 1954, it was voted to revoke the registration of Dr. George L. Lalime, Chelmsford, Massachusetts, because of ill health.

ROBERT C. COCHRANE, M.D.
Secretary
State House
Boston

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Funktionelle Atmungstherapie: Dynamik — Leistungsfähigkeit — Versagen des Atem-Stimm-Apparates. Bronchialasthma und Lungenemphysem. By Dr. med. Julius Parow, director, Institut für funktionelle Atmungstherapie der Krankenversicherungsanstalt, Berlin (West). 8°, paper, 126 pp., with 29 illustrations. Stuttgart: Georg Thieme, 1953. DM 12.90 (Distributed by Grune and Stratton, New York.)

This concise monograph on functional respiratory treatment is divided into six main parts, including the ideal and defective respiration, dilatation of the lung, bronchial asthma and treatment in general and in emergencies.

Diseases of Women. By Robert J. Crossen, M.D., assistant professor of clinical gynecology and obstetrics, Washington University School of Medicine, section head of Unit I Obstetrics and Gynecology, St. Louis City Hospital, assistant gynecologist and obstetrician, Barnes and St. Louis Maternity hospitals, assistant gynecologist, St. Louis Children's Hospital, and gynecologist and obstetrician, St. Luke's Hospital. Tenth edition. 4°, cloth, 935 pp., with 990 illustrations. St. Louis: C. V. Mosby Company, 1953. $18.50.

This standard textbook was first issued in 1907. The previous edition, printed in 1942, was reprinted six times until 1948. This edition has been throughly revised to include the latest advances in the subject. Lists of references are appended to the chapters; there is an extensive index, and the publishing is good. The book should be in all collections on gynecology.

Spatial Vectorcardiography. By George E. Burch, M.D., Henderson Professor of Medicine, Tulane University of Louisiana School of Medicine, physician-in-chief, Tulane Unit, Charity Hospital of Louisiana at New Orleans, consultant in cardiovascular diseases, Ochsner Clinic, and visiting physician, Touro Infirmary, New Orleans; J. A. Abildskov, M.D., instructor in medicine, Tulane University of Louisiana School of Medicine, and assistant visiting physician, Tulane Unit, Charity Hospital of Louisiana at New Orleans; and James A. Cronvich, M.S., professor of electrical engineering, Tulane University College of Engineering. 8°, cloth, 173 pp., with 121 illustrations. Philadelphia: Lea and Febiger, 1953. $5.00.

This book is based on an exhibit presented at the meeting of the American Medical Association at Chicago in June, 1952. It includes a summary of studies conducted at Tulane University of Louisiana School of Medicine and the Charity Hospital of Louisiana at New Orleans. A short bibliography concludes the text. The omission of an index detracts from the value of the book.

Health Yearbook 1953. Compiled by Oliver E. Byrd, Ed.D., M.D., professor of health education and director, Department of Hygiene, School of Education, Stanford University. With a foreword by David K. Brace, president, American Academy of Physical Education (1952-53) and chairman, Department of Physical and Health Education, University of Texas. 8°, cloth, 280 pp. Stanford, California: Stanford University Press, 1953. $3.50.

This yearbook, now in its eleventh year, was formerly called the *Health Instruction Yearbook.* In this issue 281 articles are abstracted from 101 different journals, special reports and other sources, the work of more than 300 authors and committees and health groups. The material is divided into 21 categories. There is a list of all the articles and indexes of authors and subjects. The series should be in all collections on the subject since it is a standard reference source.

Rh-Hr Blood Types: Applications in clinical and legal medicine and anthropology. Selected articles in immunohematology. By Alexander S. Wiener, M.D., senior serologist, office of the Chief Medical Examiner of New York City, assistant professor, Department of Forensic Medicine, New York University Postgraduate Medical School, attending immunohematologist, Jewish Hospital of Brooklyn, and attending transfusionist, Adelphi Hospital, Brooklyn. 4°, cloth, 763 pp., with illustrations and tables. New York: Grune and Stratton, 1954. $11.50.

The average physician needs and would welcome a complete discussion or a condensed review of the Rh-Hr blood types about which so much has been written in the past dozen years. Unfortunately, this book does not fulfill such a need. It is merely a collection of 84 reprints by one of the ranking serologists in the country, who has contributed a large number of articles on this subject. Even the selection of these has not been good. They merely reiterate the controversies of nomenclature and fail to clear up the present confusion in the Rh-Hr blood types. The author has made no effort to review and condense his own or other work and to bring it up to date. This collection of reprints can therefore have little more than historical value. It cannot be recommended.

From Fish to Philosopher. By Homer W. Smith, M.D., professor of physiology, New York University College of Medicine. 8°, cloth, 264 pp., with 12 illustrations. Boston: Little, Brown and Company, 1953. $4.00.

Dr. Smith traces the evolution of man through the evolution of the kidney—from the protovertebrates to the mammals and man. The text is based partly on studies in comparative physiology of the kidney made by the author during his thirty years of research. It is the study of the earth and life through 600,000,000 years of evolution. There is a special chapter on consciousness. The bibliography and technical notes, arranged by chapters, occupy 42 pages. There is a good index, and the book is well published.

Hypertensive Diseases: Causes and control. By Henry A. Schroeder, M.D., associate professor of medicine and director, Hypertension Division, Department of Internal Medicine, Washington University School of Medicine, and assistant physician, Barnes Hospital, St. Louis, Missouri. 8°, cloth, 610 pp., with 164 illustrations and 3 colored plates. Philadelphia: Lea and Febiger, 1953. $10.00.

Dr. Schroeder bases his book on a long-term study of arterial hypertension with the objective of developing a specific therapy. He discusses the etiology, pathogenesis, clinical types, diagnosis and treatment. Dr. Gressel writes on

emotions and personality in relation to hypertension, Dr. Perry on compounds of nitrogen, Dr. Davies on harmonal factors, and Dr. Gibbs on pheochromocytoma. Bibliographies are appended to the chapters. There are indexes of authors and subjects, and the publishing is excellent. The book should be in all medical libraries and in all private collections on the subject.

Anatomy and Surgery of Hernia. By Leo M. Zimmerman, M.D., professor of surgery and co-chairman, Department of Surgery, Chicago Medical School, and attending surgeon, Michael Reese, Cook County and Chicago Memorial hospitals; and Barry J. Anson, Ph.D. (Med. Sc.), professor of anatomy, Northwestern University Medical School, and member of attending staff, Passavant Memorial Hospital. 4°, cloth, 374 pp., with 204 illustrations. Baltimore: Williams and Wilkins Company, 1953. $10.00.

This new book on hernia is comprehensive in scope and includes all types, with special emphasis on the two common forms, inguinal and femoral. The studies of the anatomy of the abdominal wall are based on the observations made on a large number of actual dissections. The pertinent literature has been surveyed, and lists of references are appended to the chapters. The publishing is excellent, and the book is well illustrated. It should be in all medical libraries and in the collections of surgeons.

The Management of Pain: With special emphasis on the use of analgesic block in diagnosis, prognosis, and therapy. By John J. Bonica, M.D., director, Department of Anesthesia, Tacoma General and Pierce County hospitals, clinical associate, Department of Anatomy, University of Washington Medical School, Seattle, Washington, senior consultant in anesthesiology, Madigan Army Hospital, American Lake Veterans Administration Hospital, Western State Hospital, Northern Pacific Hospital, Doctors Hospital, and United States Penitentiary, Tacoma, Washington. 4°, cloth, 1533 pp., with 785 illustrations. Philadelphia: Lea and Febiger, 1953. $20.00.

This comprehensive treatise on pain and its management is divided into 6 main categories and again subdivided into special chapters on fundamental considerations; methods used — the analgesic block and others; pain syndromes, including pain of neurogenic origin — neuralgias, causalgia and related conditions; and pain consequent to peripheral vascular disease, of somatic origin, of visceral origin and allied disorders, and associated with cancer and other neoplasms. The introduction is a short history of the subject. Lists of references are appended to the chapters, and there is an extensive index. This valuable reference book should be in all medical libraries and available to all physicians and surgeons. It is not out of date before publication, containing as it does fundamental information. The price is not excessive for the size of the volume.

An Atlas of Pelvic Operations. By Langdon Parsons, M.D., professor of gynecology, Boston University School of Medicine, chief, Department of Gynecology, Massachusetts Memorial Hospitals, gynecologist, Palmer Memorial Hospital, and gynecologist, Massachusetts Department of Public Health and Hospital for Cancer at Pondville, Massachusetts; and Howard Ulfelder, M.D., assistant clinical professor of gynecology, Harvard Medical School, assistant surgeon, Massachusetts General Hospital, gynecologist, Massachusetts Department of Public Health and Hospital for Cancer at Pondville, Massachusetts. With illustrations by Mildred B. Codding, M.A., surgical artist, Department of Surgery, Harvard Medical School and Peter Bent Brigham Hospital, Boston. 4°, cloth, 231 pp., with 197 plates. Philadelphia: W. B. Saunders Company, 1953. $18.00.

The authors present the operations of choice in their institutions and those in common use. The contents are divided into three parts: abdominal operations; vaginal and perineal operations; and operations for carcinoma. The last part, on radical surgery, is included as a separate unit because the surgery of malignant conditions differs in scope and magnitude from that of benign tumors. The various operations are illustrated with drawings accompanied by step-by-step instructions. There is an index, and the publishing is good. The price is not excessive for this type of book, which should be in all collections on the subject.

Streptococcal Infections. Edited by Maclyn McCarthy. Symposium held at the New York Academy of Medicine, February 25 and 26, 1953. 8°, cloth, 218 pp., with illustrations. New York: Columbia University Press, 1954. $5.00. (*Symposia of the Section of Microbiology,* New York Academy of Medicine, No. 7.)

The fifteen papers comprising this volume cover the various aspects of streptococcal disease, including biology (clinical, epidemiologic and preventive) and therapy. Bibliographies are appended to the papers, and each paper provides an up-to-date summary of its subject. The series issued by the Academy should be in all medical libraries.

The Practice of Balanced Anesthesia. By Sylvan M. Shane, D.D.S., attending anesthesiologist, Lutheran Hospital of Maryland, and chief of anesthesiology, Doctors Hospital of Baltimore. With a preface by Juan White Morquecho, M.D. 8°, cloth, 196 pp. Baltimore: Lowry and Volz, 1953. $5.75.

Dr. Shane presents a summary of the present knowledge of balanced anesthesia, with a historical review of the subject. There is a bibliography of 197 references. The text is divided into four parts: general and regional balanced anesthesia; special problems; history; and the evolution of the procedure. An anesthetic is described that has been used successfully in more than 10,000 cases. The lack of an index detracts from the value of the book.

A Primer of Congestive Heart Failure. By George E. Burch, M.D., Henderson Professor of Medicine, Tulane University of Louisiana School of Medicine, physician-in-chief, Tulane Unit, Charity Hospital, consultant in cardiovascular diseases, Ochsner Clinic, and visiting physician, Touro Infirmary, New Orleans. 8°, cloth, 126 pp., with 15 figures and 1 table. Springfield, Illinois: Charles C Thomas, 1954. $4.00. (Publication No. 190, *American Lecture Series.*)

Dr. Burch discusses the mechanism and management of congestive heart failure, one of the most common diseases. Three of the chapters—more than half the text—deal with treatment. Separate chapters are devoted to two remedies used most often: digitalis and the mercurial diuretics. The primer has been written for the student, the young graduate and the general practitioner of medicine. Lists of references are appended to the four chapters, and there is an index.

Meningiomas of the Posterior Fossa. By Francesco Castellano and Giovanni Ruggiero. 8°, paper, 177 pp., with 129 illustrations. Stockholm: Acta Radiologica, 1953. Sw. Kr. 30; bound Sw. Kr. 35 — (Supplement 104 to *Acta Radiologica.*)

The author has analyzed a series of 71 cases of this rare condition observed in the neurosurgical and roentgenologic departments of the Serafimer Hospital, Stockholm, Sweden, during the period 1925-1951. The literature on the subject has been surveyed, and there is a bibliography of 182 references. The monograph is well illustrated, and there is a good index.

The Cutaneous Manifestations of Systemic Diseases. By John G. Downing, M.D., professor of dermatology and syphilology, Tufts College Medical School, professor of dermatology, Boston University School of Medicine, physician-in-chief, Unit of Diseases of the Skin, Boston City Hospital, dermatologist-in-chief, Massachusetts Memorial, St. Elizabeth's, St. Margaret's and St. Joseph's hospitals, and consultant in dermatology, New England Medical Center, Metropolitan

State Hospital and United States Public Health Service. 8°, cloth, 146 pp., with 52 illustrations. Springfield, Illinois: Charles C Thomas, 1953. $4.25. (Publication No. 182, *American Lecture Series.*)

The author, a well known dermatologist, has summarized lectures delivered at two medical schools, and the material is based on thirty years' observation in Boston hospitals. Dr. Downing stresses the importance of early recognition and proper treatment of skin eruptions occurring in connection with systemic diseases. The text is divided into 13 chapters; there is a list of references and a very good index. This monograph should be available to the general practitioner.

Review of Physiological Chemistry. By Harold A. Harper, Ph.D., professor of biochemistry, University of San Francisco, lecturer in surgery, University of California School of Medicine, San Francisco, and biochemist consultant, Metabolic Research Facility, United States Naval Hospital, Oakland and St. Mary's Hospital, San Francisco. Fourth edition. 4°, paper, 328 pp., with 29 tables and 15 illustrations. Los Altos, California: University Medical Publishers, 1953. $4.00. (*Lange Medical Publications.*)

This review, first published in 1939, has been revised and expanded in this fourth edition. It is intended to serve as a supplement to the standard textbooks on biochemistry and as a companion book for students. It has been translated into Spanish. There is a good index.

The Practical Management of Diabetes. By Edward Tolstoi, M.D., associate professor of clinical medicine, Cornell University Medical College, attending physician and chief, Diabetic Hospital of the New York Hospital, consulting physician, New York Infirmary for Women and Children, and consulting physician, Norwalk Hospital, Norwalk, Connecticut. 8°, cloth, 93 pp. Springfield, Illinois: Charles C Thomas, 1953. $3.25. (Publication No. 199, *American Lecture Series.*)

The author describes and discusses his method of treatment of diabetes with protamine insulin that he has used for the past fifteen years. There is a bibliography of 70 references.

Narcotics and Narcotic Addiction. By David W. Maurer, Ph.D., professor of English and the humanities, University of Louisville, lecturer on narcotic addiction and criminal argots, Southern Police Institute, Louisville, Kentucky; and Victor H. Vogel, M.D., medical officer in charge, European activities, United States Public Health Service, Paris, France. 8°, cloth, 303 pp., with 9 illustrations and 10 tables. Springfield, Illinois: Charles C Thomas, 1954. $7.50. (Publication No. 169, *American Lecture Series.*)

This comprehensive monograph deals with the clinical, legal and criminal aspects of narcotic addiction. It is written especially for Government officials and law-enforcement officers, social workers, judges, attorneys, the clergy and other interested persons. Three chapters deal with opiates and their synthetic equivalents, nonopiate sedatives considered to cause addiction and stimulant drugs. The remaining chapters have to do with the identification of drugs and proof of addiction, treatment, legal controls, narcotic addiction, crime and youth. The text is concluded with a glossary of slang terms commonly used by underworld drug addicts. This unusual book should be in all collections on the subject.

The Digestive Tract in Roentgenology. By Jacob Buckstein, M.D., assistant professor of clinical medicine, Cornell University Medical College, visiting roentgenologist (Alimentary Tract Division), Bellevue Hospital, New York City, attending gastroenterologist, Beth David Hospital, New York City, and consultant, Central Islip State Hospital, New York, Norwalk General Hospital, Norwalk, Connecticut, and Good Samaritan Hospital, Suffern, New York. In 2 volumes. 4°, cloth, Vol. 1, 543 pp., with 422 illustrations, Vol. 2, 659 pp., with 475 illustrations. Philadelphia: J. B. Lippincott Company, 1953. $30.00 for the set.

The first edition of this comprehensive special work was published in 1948. The author in this new edition has added a large amount of material and has brought the literature up to date. Lists of references of varying lengths are appended to the 65 chapters, and there are indexes of authors and subjects. This work presents an over-all survey of the present knowledge of the subject. The volumes should be in all collections on the digestive tract and roentgenology.

Professional Nursing: Trends and relationships. By Eugenia K. Spalding, R.N., M.A., D.H.L., professor of nursing education, Division of Nursing Education, Teachers College, Columbia University. Fifth edition. 8°, cloth, 636 pp., with 52 illustrations. Philadelphia: J. B. Lippincott Company, 1954. $5.00.

This comprehensive book on nursing as a profession was first published in 1939. This fifth edition has been thoroughly revised, although retaining the same views on general philosophy and objectives. The text includes an introduction on problem solving, 4 units on the social and professional outlook, choosing a field and succeeding in it, professional organizations and activities, and special phases, personal and professional, including legal relations, responsibilities, problems, economic security and the development of the individual personality. Lists of references are appended to the chapters, and there is a good index. The book is well published and should be in all collections on nursing.

Vitamine, Hormone, Fermente: Ein Buch für Ärzte, Biologen und Studierende. By Dr. med. Rudolf Abderhalden, private lecturer on physiology, pathology of hormones, vitamins and enzymes, Universität Basel. Fourth edition revised. 8°, cloth, 307 pp., with 30 tables. Basel: Benno Schwabe and Company, 1953. Geb. Fr. 17.50.

This new edition of a standard work first published in 1943 has been completely revised. The book should be in all collections on the subject.

Clinical Orthopaedics, Number 2. By Anthony F. DePalma, editor-in-chief. With the assistance of 5 associate editors and a board of 6 advisory editors. 4°, cloth, 247 pp., with 232 illustrations. Philadelphia: J. B. Lippincott Company, 1953. Single number, $6.00; subscription basis, $5.00.

This new number of a valuable reference serial contains material on intramedullary nailing and on general orthopedics, including 9 articles on different orthopedic conditions. There is an index, and the publishing is excellent. The series should be in all medical libraries and in orthopedic collections.

Thoracic Surgery. By Richard H. Sweet, M.D., associate clinical professor of surgery, Harvard Medical School. Second edition. 8°, cloth, 381 pp., with 159 illustrations by Jorge R. Arroyo, M.D. Philadelphia: W. B. Saunders Company, 1954. $10.00.

This well known book by a recognized authority was first published in 1950. This second edition has been revised, and the subject brought up to date; the revision includes new procedures and alterations in others, making it necessary to reset the entire text. Also, the illustrations have been revised. This is a thoroughly practical book by a master in his field, and is not burdened by superfluous bibliographic citations. The publishing is excellent, and the book is recommended for all medical libraries and to surgeons interested in the subject.

Nerve Impulse: Transactions of the Fourth Conference, March 4, 5 and 6, 1953, Princeton, New Jersey. Edited by David Nachmansohn, M.D., associate professor of neurology, Columbia University College of Physicians and Surgeons. 8°,

cloth, 224 pp., with 54 illustrations. New York: Josiah Macy, Jr., Foundation, 1954. $4.00.

The subjects discussed at this conference were the mechanism of visual, auditory and sensory receptors. Twenty-two persons took part in the proceedings. Lists of references are appended to the papers. These publications of the Foundation are essential reference sources.

Thoracic Surgery and Related Pathology. By Gustaf E. Lindskog, M.A., M.D., William H. Carmalt Professor of Surgery, Yale University School of Medicine, and surgeon-in-chief, University Service, Grace-New Haven Community Hospital; and Averill A. Liebow, M.D., professor of pathology, Yale University School of Medicine, and pathologist-in-chief, University Service, Grace-New Haven Community Hospital. 8°, cloth, 644 pp., with 285 illustrations. New York: Appleton-Century-Crofts, Incorporated, 1953. $15.00.

This new book summarizes the available knowledge on thoracic surgery and related conditions. Dr. William E. Bloomer writes on the respiratory function and its clinical evaluation, Dr. Frederick C. Waring, Jr., on the treatment of pulmonary tuberculosis, including therapeutic pneumothorax, oleothorax and pneumoperitoneum, and Dr. Ralph D. Alley on preoperative preparation, operative and postoperative care. Lists of references are appended to the chapters, and there is a good index. The publishing is excellent, and the book is recommended for all medical libraries and to surgeons interested in the subject.

Maternal Dependency and Schizophrenia: Mother and daughters in a therapeutic group. A group-analytic study. By Joseph Abrahams, M.D., and Edith Varon, M.A., M.S. 8°, cloth, 240 pp. New York: International Universities Press, Incorporated, 1953. $4.00.

This report presents a study of a group of 7 mothers and daughters. The research was done at St. Elizabeth's Hospital, Washington, D. C., with funds supplied by the Veterans Administration. There is an appendix on group psychotherapy carried out with members of families, a procedure that began as early as 1943, and a bibliography on this method of treatment. The text concludes with a bibliography of the Veterans Administration Group Psychotherapy Research Project.

Clinical Endocrinology. By Karl E. Paschkis, M.D., associate professor of medicine, assistant professor of physiology and director of the Division of Endocrine and Cancer Research, Jefferson Medical College, chief of Endocrine Clinic, Jefferson Medical College Hospital, and attending endocrinologist, St. Christopher's Hospital for Children, Philadelphia; Abraham E. Rakoff, M.D., clinical professor of obstetric and gynecologic endocrinology, Jefferson Medical College, endocrinologist to the Hospital Laboratories, Jefferson Medical College Hospital, and guest lecturer in gynecic endocrinology, Department of Internal Medicine, University of Pennsylvania School of Medicine; and Abraham Cantarow, M.D., professor of biochemistry, Jefferson Medical College. 8°, cloth, 830 pp., with 253 illustrations. New York: Paul B. Hoeber, Incorporated, 1954. $16.00.

In this new book on endocrinology the authors discuss the various endocrine organs and their anatomy, physiology and diseases. There are chapters on obesity and on procedures and methods, and the text concludes with a useful list of commercial hormone preparations. Bibliographies are appended to the chapters, and the pertinent literature is noted throughout the text. There is an extensive index, and the volume is well published.

Pneumonia. By Hobart A. Reimann, M.D., visiting professor of medicine, American University of Beirut, Lebanon. 8°, cloth, 236 pp., with 16 illustrations. Springfield, Illinois: Charles C Thomas, 1954. $5.75. (Publication No. 160, *American Lecture Series.*)

In this monograph the author summarizes all the various types of pneumonia. Special attention is given to the pneumococcal, viral and new types of the disease. The etiology, pathogenesis, pathology, symptoms, prevention and treatment are discussed in that order. References are appended to the section on each type of pneumonia, and there is a good index.

Connective Tissues: Transactions of the Fourth Conference, February 18, 19 and 20, 1953, Princeton, New Jersey. Edited by Charles Ragan, M.D., associate professor of medicine, Columbia University, College of Physicians and Surgeons. 8°, cloth, 197 pp., with 61 illustrations. New York: Josiah Macy, Jr., Foundation, 1953. $3.75.

The participants in this conference discussed the general areas of agreement reached in the conference group, isolation and characterization of mammalian striated myofibrils, the effect of vitamin A on organ cultures of skeletal and other tissues, and the outline of problems to be solved in the study of connective tissues. Eleven persons took part in the conference. Lists of references are appended to the papers.

"Unternehmerkrankheit," Entstehung und Verhütung. By Prof. Dr. Med. M. Hochrein, and Doz. Dr. Med. Habil. I. Schleicher. 8°, paper, 60 pp., with 17 illustrations and 3 tables. Stuttgart: Georg Thieme, 1953. DM 4.80. (Distributed by Grune and Stratton, New York.)

The authors in this interesting monograph discuss the etiology and prevention of the so-called manager's disease, affecting executives between the ages of fifty and sixty years. The text is divided into 2 main parts: diseases of workers and the prevention of circulatory disturbances. A number of interesting tables are presented in the first part. One shows the span of life of 18 years, in the early iron and bronze period, to 66.8 years in 1947. Two others depict the deaths during the period from 1910-1940, and days lost from work, and both show that heart and cardiac-kidney conditions lead all other diseases. An analysis of 157 cases of heart conditions, during the years 1949-1952, showed that executives and professional persons comprise 45 per cent. This important monograph should be in collections on industrial medicine and cardiology.

Regional Block: A handbook for use in the clinical practice of medicine and surgery. By Daniel C. Moore, M.D., director, Department of Anesthesiology, Mason Clinic, and chief of anesthesia, Virginia Mason Hospital, Seattle, Washington. 4°, cloth, 373 pp., with 262 illustrations. Springfield, Illinois: Charles C Thomas, 1953. $11.00.

This book is written primarily for the general practitioner and the beginner in anesthesiology and therefore does not cover all phases and methods of regional anesthesia. The material is divided into three parts: fundamental considerations; nerve-block anesthesia; and spinal (subarachnoid) and caudal (epidural) analgesia. Step-by-step illustrations of procedures are featured. There is a good index. The book should be in collections on the subject.

The Principles of Thoracic Anaesthesia: Past and present. By William W. Mushin, M. A. (Oxon.), M.B., B.S. (Lond.), M.R.C.S., F.F.A.R.C.S., D.A., director of anesthetics, Welsh National School of Medicine, consultant anesthetist, United Cardiff Hospitals, and consultant adviser in anesthetics, Welch Regional Hospital Board; and L. Rendell-Baker, M.B., B.S. (Lond.), M.R.C.S., D.A., consultant anesthetist, United Cardiff Hospitals and Welsh Regional Hospital Board, and first assistant, Department of Anaesthetics, Cardiff. 8°, cloth, 172 pp., with 193 illustrations. Springfield, Illinois: Charles C Thomas, 1953. $9.50.

This excellent monograph considers the general subject of thoracic anesthesia, with special emphasis on the instruments and apparatus used. The text is divided into 3 parts: the pneumothorax problem and its solution; the historical background; and methods in use today. Lists of references are appended to the chapters, and there is a good index of authors and subjects. The text is extensively illustrated.

The printing was done in Great Britain by A. R. Mowbray and Company, Oxford, and the publishing is excellent. The book should be in collections on anesthesia and thoracic surgery.

NONCLINICAL NOTES

APPOINTMENT OF DR. ELKIN

Dr. Milton Elkin, of Boston, has been appointed professor of radiology and chairman, Department of Radiology, Albert Einstein College of Medicine of Yeshiva University, New York City. Dr. Elkin received his degree from Harvard Medical School in 1941.

RHODE ISLAND HOSPITAL APPOINTMENT

Dr. Henry McCusker has been appointed assistant director, Rhode Island Hospital, and director, Department of Post-Graduate Medical Education.

Dr. McCusker was formerly surgeon-in-chief, Department of Orthopedic Surgery and Fractures, Rhode Island Hospital, and president, Rhode Island Hospital Staff Association, and for the past year has been consulting orthopedic surgeon for several Rhode Island hospitals.

VETERANS ADMINISTRATION HOSPITAL MEDICAL TRAINING PROGRAM

A residency-training program and other professional educational training will be instituted at the Veterans Administration Hospital, East Orange, New Jersey, about July 1, under the direction of a medical advisory committee of which Dr. Bernard J. Pisani of Englewood, New Jersey, is chairman.

MEAD JOHNSON SCHOLARSHIP AWARD

The Mead Johnson General Practice Scholarship Award was given to Dr. John T. Kaemmerlen, Jr., of the graduating class of Boston University School of Medicine. This scholarship of $1000 will be applied to a year of residency in general practice after the completion of a year's internship.

The scholarship-award program is administered by the American Academy of General Practice, who have made identical awards, furnished by Mead Johnson Company, to nine other medical-school seniors and to ten residents.

HARVARD MEDICAL SCHOOL PROFESSORSHIPS

Dr. Eric Lindemann has been appointed professor of psychiatry, Harvard Medical School, and psychiatrist-in-chief, Massachusetts General Hospital.

Dr. Raymond DeLacy Adams has been appointed Bullard Professor of Neuropathology, Harvard Medical School, and continues as chief, Neurologic Service, Massachusetts General Hospital.

NOTICES

ANNOUNCEMENT

Dr. Simon Horenstein announces the opening of an office for the practice of neurology at 520 Beacon Street, Boston, Massachusetts.

LABORATORY REFRESHER TRAINING COURSES

The schedule of the Laboratory Refresher Training Courses, of the Department of Health, Education and Welfare, to be given at the Communicable Disease Center in Chamblee, Georgia, has been announced. Information may be obtained by writing the Laboratory Training Services, Communicable Disease Center, United States Public Health Service, P. O. Box 185, Chamblee, Georgia.

SANITARY ENGINEERING TRAINING PROGRAM

A radiologic health training program at the Robert A. Taft Sanitary Engineering Center, Cincinnati, Ohio, will be sponsored by the Public Health Service, U. S. Department of Health, Education and Welfare from November, 1954 through May, 1955. The program, on the hazards of radiation, is designed primarily for professional personnel of State and local health departments, but other qualified applicants may apply. Further information may be obtained from the chief, Radiological Health Training Section, Robert A. Taft Sanitary Engineering Center, 4676 Columbia Parkway, Cincinnati 26, Ohio.

AMERICAN UROLOGICAL ASSOCIATION AWARD

The American Urological Association announces the annual award of $1000 (first prize $500, second prize $300 and third prize $200) for essays on the result of clinical or laboratory research in urology. Competition is limited to urologists not more than ten years from graduation and to men in training to become urologists. The essay awarded first prize will be presented at the meeting of the American Urological Association, Biltmore Hotel, Los Angeles, May 16-19, 1955. Essays must be received by the secretary before January 1, 1955. Further information may be obtained from the secretary, William P. Didusch, 1120 North Charles Street, Baltimore, Maryland.

SOCIETY MEETINGS AND CONFERENCES

July 21–August 23. Consultation Clinics for Crippled Children in Massachusetts. Page 1054, issue of June 17.

July 22 and 23. International College of Surgeons. Regional Meeting. Page 828, issue of November 12.

July 23–29. International Cancer Congress. Page 914, issue of November 26.

July 26–31. International Congress of Gynecology and Obstetrics. Page 400, issue of March 4.

August 1–7. Pan-American Congress of Pediatrics. Page 850, issue of May 13.

August 17–20. Argentine Congress of Thoracic Surgery. Page 708, issue of April 22.

September 6–10. International Poliomyelitis Congress. Page 399, issue of March 4.

September 6–11. University of Illinois College of Medicine. Annual Assembly in Otolaryngology. Page 1092, issue of June 24.

September 7–10. Nineteenth Annual Congress of the United States and Canadian Sections of the International College of Surgeons. Page 828, issue of November 12.

September 12–15. Second International Congress of Cardiology. Washington, D. C.

September 13–15. American Association of Blood Banks. Page 968, issue of June 3.

September 16–18. American Heart Association. Annual Scientific Sessions. Washington, D. C.

September 22. New England Pediatric Society. Page 968, issue of June 3.

October 1 and December 3, 1954; February 4 and April 1, 1955. New England Society of Anesthesiologists. Page 1054, issue of June 17.

October 7 and 8. Pan-Pacific Surgical Association. Page 1092, issue of June 24.

October 8 and 9. Academy of Psychosomatic Medicine. Page 748, issue of April 29.

October 11–15. American College of Physicians Course. Page 44, issue of July 1.

October 18–22. American Occupational Therapy Association. Page 1092, issue of June 24.

October 18–29. New York Academy of Medicine Graduate Fortnight. Page 44, issue of July 1.

October 25–27. New England Postgraduate Assembly. Hotel Statler, Boston.

October 27. New England Obstetrical and Gynecological Society. Annual Meeting. Hotel Somerset, Boston.

October 27–29. International Symposium on the Hypophyseal Growth Hormone. Page 1092, issue of June 24.

October 31–November 4. American Institute of Dental Medicine. Page 968, issue of June 3.

November 1954–May 1955. Sanitary Engineering Center Training Programs. Notice above.

(Notices concluded on page xxi)